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# The American Journal of Surgery

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A PRACTICAL JOURNAL BUILT ON MERIT

## EDITORIALS

### INTRODUCTION

THIS Symposium of Obstetrics has been made possible by the support of the Editor of The American Journal of Surgery and the efforts and coöperation of the various contributors.

The field of obstetrics is assuming a constantly increasing importance in medical education and practice. This is true because it has come to be realized that there was and still is much unnecessary loss of health and life associated with the vital and essentially physiologic processes of human reproduction.

Ignorance and lack of adequate care due to many factors have played important parts in contributing to these disabilities and deaths of mothers and infants. It has been a controversial matter as to whether or not these results could be improved. This can be no longer a matter for argument as statistics now prove that the lives of mothers and newborn infants can be saved by disseminating knowledge and by providing more adequate care for women during pregnancy, labor, and the puerperium and for the newborns during the antenatal, intranatal and postnatal phases of their existence.

When the maternal mortality rate per 10,000 live births can be reduced from 69 in 1928 to 43.5 in 1938, the stillbirths from 39 in 1927 to 33 per 1000 live births in 1937 and the neonatal death rate per 1000 live

births from 36.1 in 1927 to 31.3 in 1937, there is no longer a valid argument against the possibility of reducing the number of deaths.

It is apparent that the mortality rates can be improved by the general application of the knowledge we already have. It is still undetermined how great a reduction in deaths is possible. It has already been demonstrated in certain states that the general rate can be reduced 50 per cent, though thus far the rate for the registration area has been cut something over 25 per cent. There are local statistics showing that the maternal mortality rate can be reduced to as low a figure as 1 per 1000 live births and even less. It could reasonably be anticipated that with adequate consecutive care by competent personnel with essential equipment not more than one pregnant woman in a thousand need lose her life during the pregnancy, the labor and the puerperium.

There is an unnecessary loss of fetal and infant life which can be markedly reduced. The combined stillbirth and neonatal death rates now equal about 70 per 1000 live births. There is sufficient evidence to prove that with complete and adequate prenatal, natal and postnatal care these combined rates could be brought down to 35. What possibilities open up with the application of new knowledge requires a prophetic

instinct which cannot be based on any scientific data. While individuals are doomed to die ultimately there would seem to be little justifiable reason for a healthy woman to die while carrying out a biologic and physiologic process, nor would it seem necessary that the life of a fetus should be arrested in its incipency. A great deal of discussion and thought has been given to the deaths which have taken place in connection with the carrying out of the function of human reproduction. Death is a very real and tangible affair which can be used as a basis for statistical computation. Morbidity is difficult to define, to estimate and to use for statistical comparisons. Many of the causes of death may produce disability of varying degrees and duration and unquestionably the improvement of the general level of obstetric care will in addition to saving lives, lessen the disabilities associated with childbearing.

Formerly there were many genital fistulas as the result of birth injury; now they are infrequent. Congenital syphilis is of less frequent occurrence than formerly and by generally adequate care can be eliminated. These examples are definite illustrations of what has been done and are positive indications of what can be accomplished.

In attempting to secure as nearly perfect results as possible it is necessary to realize that coëxistent diseases are affected by pregnancy and its sequelae and that the course of gestation is modified by these diseases. It is of the utmost importance to know the physical and mental status of the woman who is about to be or already is pregnant. We have chosen three diseases which are quite frequently seen and which have a very intimate interrelationship with reproduction and increase the hazards of childbearing. Women who have venereal, tuberculous or cardiac diseases require special attention and treatment even though no pregnancy is present, but when the two conditions coëxist the required attention is definitely increased. Even early pregnancy presents certain hazards which are inherent in the pregnancy itself.

Ectopic pregnancy is a very critical condition and has to be recognized and treated promptly to avoid disaster. It is difficult to diagnose even when it presents acute symptoms of rupture. Stress upon its diagnosis with early institution of hospitalization and of surgical treatment are definitely in order. Abortion is a manifold problem both from medical and sociologic points of view. It is not possible to give accurate data relative to the annual number of abortions which occur in our country, but there must be 750,000 or so. Many of these are unavoidable with our present knowledge and they often cause much grief in a family desirous of having children. On the other hand the intentional abortions are numerous and they result, in many a fatality which could be avoided, and cause much disability and subsequent sterility from infection. Those women who desire children should accept a pregnancy when it comes and not attempt postponement to some more convenient time at the expense of fetal life and of a hazard of greater or less risk of death and of disability to themselves. The importance of prenatal care and preparedness is illustrated by the causes of obstetric hemorrhage. The well being of mother and fetus is promoted by observation of the maternal nutritional state and by supervision of diet under both normal and abnormal conditions.

Labor is the crucial period during which the fate of both mother and baby may be determined within a few moments. It is important that the doctor be sure of his ground and not yield to the importunities of relatives and patient for an easy or short labor rather than one safe for mother and infant. One cannot compromise judgment which involves health and life. Two lives hang in the balance and one should not tip the scales to cheat nature but so adjust them as to assist her. The Symposium continues to give a pictured outline of the normal and abnormal aspects of labor with some consideration of prevention and repair of complications such as hemorrhage and laceration.

Infections do arise and, while prophylaxis remains of the greatest importance, nevertheless great progress has been made in their treatment. The newborn cannot be regarded as an obstetric by-product, and if its fate is not determined during pregnancy and labor the first few moments of extra-uterine existence may decide between life and death or between a normal and a handicapped existence. The establishment of respiration is vital but it should be normal. It is of little use to have breathing

established artificially and then have death from pneumonia or pneumothorax follow a few days after.

No attempt has been made to present complete expositions of the various subjects included in this symposium to say nothing of writing a comprehensive document on obstetrics. We have tried to indicate the field covered and to outline some of the frequent and outstanding problems in present day obstetric practice.

FRED L. ADAIR, M.D.

## THE CHANGING ASPECTS OF GYNECOLOGY

THE papers which are included in this Symposium on Gynecology may, I believe, be considered truly representative, not only from the standpoint of the authors but also as regards the topics which are discussed. Certainly they exemplify the changing aspects of gynecology, and emphasize the fact that it can no longer be considered a mere subdivision of surgery, as seemed to be the tendency not so many years ago. As a matter of fact, only a small proportion of gynecological patients nowadays are in need of surgical procedures. Sometime ago I happened to sit in on a discussion of this very point by a group of prominent gynecologists. All agreed that the proper management of most gynecological cases does not call for surgery, none placing the proportion of surgical cases above 10 per cent, and most of them at considerably less.

A large proportion of our nonsurgical patients, though not by any means all, are those presenting various functional disorders, especially of endocrine nature. The development of gynecological endocrinology and the increasing interest in the general biologic aspects of our specialty constitute the most outstanding contribution of the present generation to gynecology. Just as the preceding era was characterized by an awakened interest in the pathologic aspects of gynecological disease, and a still earlier one by that remarkable development of

gynecological surgery to which subsequent years have added so little, so may we now properly consider ourselves in a physiologic or biologic era of gynecology.

Both pathology and surgery are still, as they will always be, of fundamental importance in the training and practice of the gynecologist. Not all the surgical and pathologic problems of our specialty have been solved, and some of these, such as the applicability and technique of vaginal hysterectomy, the still much discussed question of total versus subtotal hysterectomy, and the early diagnosis of cancer are discussed in this symposium by outstanding authorities.

In the same way, the fascinating and intricate though as yet imperfectly understood problems of gynecological endocrinology are presented by authors selected because of their contributions and accomplishments in this potentially rich new field.

One does not need to be an old man to reminisce on the amazing advances which have been made during the past generation in our knowledge of the physiology of the reproductive cycle. It seemed so simple to our immediate forbears to explain menstruation as due to an internal secretion of the ovary, though this explanation seemed rather nebulous since nothing was known as to the source or nature of this secretion. Now, on the other hand, our concepts are



made concrete by the fact that both of the ovarian hormones have been isolated, that we know the exact chemical composition of both, and that both can be prepared in crystalline form, so that they can be handled much as we handle drugs, especially since we know a good deal as to their physiologic effects.

We have learned much too, as to the interrelationship of ovarian function with that of other endocrine glands, especially the pituitary, so that we no longer conceive of the menstrual cycle as a purely pelvic phenomenon, but think of it rather as embracing far-flung and deeply seated constitutional changes, which include certain conspicuous pelvic phenomena whose ultimate purpose is the propagation of the race. In the study of all the cogs in this complex machinery there have been rich opportunities for the clinician, the anatomist, the physiologist, and the biochemist, and all have made rich contributions. And

yet there is a general feeling that the surface has been merely scratched and that many rich nuggets will be uncovered by the intensive work now being devoted to all aspects of the general problem.

No apology seems necessary, therefore, for including in this Symposium a considerable number of papers devoted to the consideration of functional or endocrine problems, particularly in view of the authoritativeness of these presentations. The other topics have all been selected because of their present day interest, and all are discussed by writers whose names are identified with the subjects which they present. If this number of THE AMERICAN JOURNAL OF SURGERY is read by one of our successors a hundred years hence, it should convey a correct picture of the type of gynecological problems which engage the interest and attention of the gynecologist of today.

EMIL NOVAK, M.D.



# OBSTETRICS AND GYNECOLOGY SYMPOSIUM

## OBSTETRICS

EDITED BY

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# PRECONCEPTIONAL CARE

FRED L. ADAIR, M.D.

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CHICAGO, ILLINOIS

**P**RECONCEPTIONAL care is designed to assist in securing perfect reproduction. It rests upon fundamental eugenic and euthenic principles. It is that care and attention which is given prior to conception and involves the elimination of those individuals who are not suitable for wholesome reproduction and the selection of those who are capable of normal reproduction. This elimination and selection must be based on known biologic principles which can be best adapted to humanistic, ethical, social and economic customs and laws. The application of the principles must fit into the legitimate and proper needs and desires of individuals and of society. It is a part of complete maternal care, but includes the examination and care of both the male and the female. After conception occurs the essential attention involves primarily the prospective mother and the fetus during pregnancy and labor, and of the mother and newly born infant as more or less completely independent individuals. One may, therefore, include the entire program under the general title of Maternal Care or Welfare, as the mother is the keystone of the complete arch of human propagation.

In defining Maternal Care it must be borne in mind that in order to be complete and competent the attention given to the mother must be such that it will both directly and indirectly enable her to carry out the physiologic process of reproduction in as nearly normal a manner as possible. This implies the maintenance of the integrity of the family and insures the reproduction of normal offspring in sufficient numbers to preserve the human race and promote its advancement.

In order to secure a survey of the field of endeavor and place preconceptional care

in its proper sphere, it is important to understand the different phases of the program of Maternal Care.

1. Preconceptional care includes all the eugenic and euthenic attention which is necessary to determine the fitness of individuals to bear children and to prepare them for conception and to protect the offspring, during both intra-uterine and extra-uterine life, from detrimental influences which might subsequently interfere with a normal and reproductive life.

2. Antenatal, prenatal and antepartum all refer to the care given to the prospective mother and to the fetus during gestation. The first and second terms refer more specifically to the fetus while the last one designates the mother as the particular object of attention.

3. Natal, intranatal, intrapartum and delivery care apply to the care and attention given to the mother and the fetus during labor. The first two words refer more particularly to the welfare of the fetus and the latter two terms apply to the mother. Usually their interests are mutual, but sometimes they are in conflict.

4. Postnatal and postpartum care are quite distinct in that the mother and the infant become independent individuals. The care is quite divergent and while the two live in a sort of symbiosis they are physically separate from one another. This independence normally develops progressively as the weeks, months and years pass. The care of both may be divided into the immediate and the remote. With regard to the mother this postpartum care immediately assumes an aspect which is related to preconceptional care. It is important that, among other things, she be left with a desire and a capacity subsequently to carry out a normal reproductive career.

With reference to the newborn it is important to bear in mind that its growth and development carries the implication that the normal individual must be able at the proper time to reproduce normal human beings, and if possible those who are of a superior rather than of an inferior quality.

It is obvious that adequate Preconceptional Care involves a consideration not only of the potential fathers and mothers, but also of their individual progenitors. It is apparent that it includes both eugenic and euthenic backgrounds. It must be understood to include within its scope both the present and the future welfare of humanity and that the good of all is paramount to that of the one or of the few. It must sooner or later be recognized and acknowledged that it includes within its scope both contraception and procreation and that it is oftentimes as important for the welfare of one or of all to avoid conception as it is to promote conception. We should reconcile our minds and our acts to the idea that ultimately the birth rate will have to be judged not alone on a quantitative but also upon a qualitative basis. Our major concern will ultimately be not solely whether the birth rate exceeds or equals the death rate, but also whether or not the quality of those who are born and survive is better than that of those who succumb.

It is a well known fact that there has been a downward trend of the birth rate for a number of past decades. There is little evidence to support the idea that this is due to decreased fertility. The statistical data seem to indicate that just as many women are capable of reproducing but that the number of pregnancies per woman has diminished. Some studies have been made to determine which social groups tend to reproduce the fewest, and it appears that the intellectual and higher economic groups tend to have the smallest number of children. Some have argued that there is a tendency for the human race to become biologically inferior. It is very difficult, except in smaller groups of defective individuals, to erect biologic criteria of

fitness. Most of the analyses of the birth rate have been on a quantitative rather than a qualitative basis. Both are important as the live births must equal or exceed the deaths, or the human race will ultimately become extinct.

The quality is important as it must equal or exceed the present, or the human race will deteriorate. What qualities must be preserved and transmitted? They cannot be those which frequently make for economic success or for failure, as those who become rich may have undesirable qualities and those who are poor possess desirable ones. They cannot be solely intellectual as one may be brilliant and be intellectually perverted. They cannot be purely physical as one may be a giant in body but a pigmy in mind. Society is very complex in its organization, and there must be those who can fit into the different niches and carry out their functions adequately.

What should one consider as the essentials in those who are to provide the future components of the human race? First, they should be physically fit by being free from hereditary and transmissible diseases. Second, they should be mentally fit to understand and adapt themselves to life in the community of their fellows. Third, they should have character to withstand the harmful temptations of life and a willingness to work with and help their fellows rather than to profit by their exploitation.

How to accomplish these objectives is quite another matter, but beginnings are being made and gradually one idea after another will be applied and eventually the desired ends will be accomplished. We have started with the physical side first and real attempts are being made by means of premarital examinations to avoid the transmission of disease to the partner and to the offspring. More and more parents are coming to realize that good health is important, not only during pregnancy, but also at the time of conception. The application of these ideas involves two basic principles. First, the avoidance of concep-

tion at any time in those who are not adapted to normal reproduction. Second, the prevention of conception in those who are temporarily not suited for normal propagation.

At present our basis of selection rests almost entirely on physical or medical grounds. The doctors and other scientists, therefore, must assume the responsibility for this very important program of human welfare. As already indicated the decision rests upon certain eugenic and euthenic principles which have been established. One cannot and should not proceed upon theoretical considerations. Individuals with known serious hereditary defects should not reproduce their kind. Perhaps the steadily increasing stream of defectives could be arrested by this means. Transmissible disease such as syphilis could certainly be eliminated. Health and longevity could be promoted by timing a pregnancy, as in a tuberculous woman.

The methods become of importance, and obviously different procedures would be indicated for permanent and for temporary contraception. Sterilization is most appropriate for the former and contraceptive devices for the latter. The rhythm theory limits the number of gestations but is not to be relied upon in those for whom pregnancy must be interdicted either temporarily or permanently. The use of obstructive devices with or without chemical spermicides is successful where they are properly applied and consistently employed. Chemical contraception has not attained perfection and various agents for the purpose of arresting spermatogenesis are not yet satisfactory. It must be remembered that some devices are seriously harmful and disability and even death have resulted from their use.

Sterilization of the male or the female is a relatively simple procedure especially in the former, although males are difficult to convince that cutting the vas deferens is simple, safe and harmless. They are more willing to have their wives suffer an abdominal incision with ligation of the

tubes. The lumen of the tube may be occluded by a variety of methods from cauterization, ligation, resection, excision and even hysterectomy. These procedures may be carried out before any pregnancies have taken place or after one or more have occurred. They may be done to prevent the birth of a potentially defective fetus or purely in the interest of the mother's health and life.

The interruption of a pregnancy hardly should be incorporated in a discussion of preconceptional care, but a therapeutic abortion frequently presupposes that a future pregnancy is also undesirable.

It seems consistent to follow the principle that when the pregnant woman is suffering from a persistent disease which necessitates a therapeutic abortion, she or her husband should be sterilized. This would avoid the necessity for a future abortion. The solution of such a problem arises in chronic cardiac, vascular and renal diseases. If the condition is acute and recovery probable, sterilization is not indicated, but contraceptive devices should be used until recovery is complete and pregnancy safe.

Preconceptional care has been discussed from the standpoint of control of reproduction but the opposite point of view is even more important. This may be termed the preconceptional viewpoint. There are two main groups of cases which come under consideration here. First, those who are presumably capable of reproduction and, second, those who have been unable to have children.

No discussion will be given of the infant, child and adolescent care, necessary for the growth and development of normal persons, which will be assumed to have been obtained. The result should be two presumably healthy young adults contemplating marriage and the founding of a family. They come for a prenuptial or a premarital examination. Such a requirement has the force of law in some states. The law which became effective in Illinois on July 1, 1937 is quoted in the following paragraphs:

"Section 1. Section 6a of 'An Act to revise the law in relation to marriage,' approved February 27, 1874, as amended, is amended to read as follows:

"Sec. 6a. All persons making application for a license to marry shall at any time within fifteen (15) days prior to such application be examined by a physician duly licensed in this State as to the existence of or freedom from any venereal disease, and, except as otherwise herein provided, it shall be unlawful for the county clerk of any county to issue a license to marry to any person who fails to present for filing with such county clerk a certificate signed by such physician setting forth that such person to the proposed marriage is free from venereal diseases as nearly as can be determined by a thorough physical examination and such standard microscopic and serological tests as are necessary for the discovery of venereal diseases. If, on the basis of negative laboratory and clinical findings the physician in attendance finds no evidence of venereal diseases, he shall issue a certificate to the effect to the examinee, which certificate shall read as follows, to-wit:

"I, (Name of Physician) \_\_\_\_\_ being a physician, legally licensed to practice in the State of \_\_\_\_\_ (my credentials being filed in the office of \_\_\_\_\_ in the City of \_\_\_\_\_ County of \_\_\_\_\_ State of \_\_\_\_\_) do certify that I did on the \_\_\_\_ day of \_\_\_\_\_ 19\_\_\_\_ make a thorough examination of \_\_\_\_\_ and considered the result of a microscopical examination for gonococci and an approved serological test for syphilis, which was made at my request, and believe \_\_\_\_\_ to be free from all venereal diseases.

\_\_\_\_\_  
Signature of Physician

"Such certificate of negative findings as to each of the parties to a proposed marriage to which laboratory reports of microscopical examinations of smears from the genitalia for the gonococcus of gonorrhea and serologic tests for syphilis are attached, shall be filed with the county clerk of the county wherein the marriage is to be solemnized at the time application is made for a license to marry. Laboratory tests for venereal diseases required hereunder shall be tests approved by the State Department of Public Health and shall be made by laboratories of said Department or by such other laboratories as are approved by said Department. Such tests as may be made by the health

departments of cities, villages and incorporated towns maintaining laboratories shall be free of charge. The results of all laboratory tests shall be reported on standard forms prescribed by the State Department of Public Health.

"Irrespective of the results of laboratory tests and clinical examination, the clerk of the respective counties shall issue a marriage license to parties to a proposed marriage (a) when the woman is pregnant at the time of such application, (b) when the woman has, prior to the time of application, given birth to an illegitimate child which is living at the time of such application and the man making such application makes affidavit that he is the father of such illegitimate child. The county clerk shall, in lieu of the health certificate required hereunder, accept, as the case may be, either an affidavit on a form prescribed by the State Department of Public Health, signed by a physician duly licensed in this State, stating that the woman is pregnant, or a copy of the birth record of the illegitimate child, if one is available in this State, or if such birth record is not available, an affidavit signed by the woman that she is the mother of such child.

"Also irrespective of the results of laboratory tests and clinical examination, the clerks of the respective counties shall issue a marriage license to parties to a proposed marriage when, after investigation, the Director of the State Department of Public Health, or his duly authorized representative, issues or causes to be issued a certificate that such marriage may be consummated without serious danger to the health of either party to the proposed marriage or to any issue of such marriage.

"Any county clerk who shall unlawfully issue a license to marry to any person who fails to present for filing the certificate provided for in this Act or who shall refuse to issue a license to marry to any person legally entitled thereto under this Act, or any physician who shall knowingly and wilfully make any false statement in the certificate, or any party or parties having knowledge of any matter relating or pertaining to the examination of any applicant for license to marry, who shall disclose the name, or any portion thereof, except as may be required by law, shall upon proof thereof be punished by a fine of not less than \$100.00 nor more than \$500.00 for each and every offense.

"Any person who shall obtain any license to marry contrary to the provisions of this section shall, upon conviction thereof, be punished by a

fine of not less than \$100.00 or by imprisonment in the county jail for not less than three (3) months or by both such fine and imprisonment. Any license to marry issued hereunder shall be void thirty (30) days after the date thereof."

It is to be noted that this law is primarily directed toward the control and elimination of venereal disease. The law is an admirable beginning and does focus attention on certain health problems in relation to marriage. It falls far short of what should be considered essential for preconceptional and premarital examinations. An adequate investigation of this type should include a study of both prospective parents from standpoints of their heredity, of past diseases and of the present state of their health. This includes a complete history and physical examination with routine laboratory tests and special studies when indicated.

It is not fully known just what influences affect the germ cells during the process of their development and there are enormous gaps in our knowledge of human heredity. We know that certain agents can destroy the male germ cells, and it is fair to assume that the same or similar agents can injure them but probably not entirely destroy their fertilizing power. It is well known that there are many embryonic and fetal malformations and that the examination of semen of different males shows varying percentages of normal and abnormal, mature and immature germ cells. Little is known about the fertilizing power of these various types of germ cells and of the ultimate result so far as any resultant embryos are concerned. The routine examination of this secretion is not indicated but it should be done in cases of sterility, abortions and malformations. It is, of course, impossible to secure ova for examination, but modern methods show the possibility of drawing certain conclusions relative to anovulatory cycles by endometrial biopsy. The ovaries are well protected from external influences; however, toxic and infectious agents gaining

access to the maternal blood stream may affect their formation and development temporarily or permanently. The male gonads being more exposed are more susceptible to environmental influences. It has been shown that elevation of local temperature may affect spermatogenesis. It is an interesting question which should be answered as to what effect fever has on the development of ova and sperms.

This discussion indicates the importance of considering illness in relation to conception and it is not overdrawn to emphasize the importance of the parents being in good health prior to and at the time of conception. It is well known that infertility is frequently associated with poor thyroid function and that calcium and phosphorus and iodine have a relationship to productivity. If sterility can result from metabolic disturbances of this type it is only logical to assume that lesser damage to germ cells may occur and a poor offspring result. The main points of this discussion are that as a part of preconceptional care one should consider the facts that germ cells carry inescapable hereditary factors and that even though they lie protected in body tissues they are still susceptible to environmental influences.

After fertilization occurs the fate of the embryo is in part determined and the hereditary die is cast. Environmental influences can modify its intra-uterine development. The further course of development depends upon maternal environment. Preconceptional care strives to remove these detrimental factors prior to fertilization of the egg. There is no evidence that syphilis affects the male or female germ cells or that it is carried by them. The maternal environment is such that the treponema is carried to the fetus and infects it. The preconceptional diagnosis and treatment of syphilis will yield better results than recognition and care during the prenatal period. There is evidence in Connecticut and Illinois that the prenuptial tests are reducing the number of cases of congenital syphilis. Similar laws in



New Jersey, New York, and Pennsylvania will, no doubt, yield worthwhile results in controlling congenital syphilis. The transmission of syphilis from one partner to another is also important, irrespective of the possibility of the subsequent infection of the fetus and newborn.

The prevention of marital spread of gonorrhea is an even more difficult problem because the criteria for diagnosis and cure are less definite and the treatment is less specific.

Gonorrhea is not held responsible for as many fatalities as syphilis, but its ravages are not less great. The frequency of marital transmission is high and the incidence of subsequent male and female sterility as a result of its invasion is considerable. What effect it has as an etiologic factor in abortions has not been evaluated clearly, although the lesions of the cervix, corpus and tubes must be factors in the production of abnormal gestations. The amount of disability resulting in women from gonorrheal infections is very great, while the loss of reproductive function is usually irreparable and contributes largely to acquired sterility.

The other venereal diseases are less of a problem as they are limited to certain groups and, though serious in the individuals afflicted, the number of those infected is not great and the diseases are not widespread. There are also communicable diseases other than these whose transmission from one mate to another can be controlled by preconceptional care. The acute infectious diseases are usually transient and more or less general in their distribution so that only commonly recognized methods of control can be of any avail. However, such a chronic infectious disease as tuberculosis may be unrecognized even in its active contagious stage, and a man may infect his bride or she transmit the disease to him. It is important that pulmonary tuberculosis be diagnosed so that proper precautions may be taken before the hazards of marital life transmit the infection from one to the other. It is particularly important that no woman who

has an uncured tuberculosis should become pregnant.

Preconceptional care has to do with the elimination of those conditions which cause infertility or tend to reduce fertility. These involve the careful examination of both male and female and even then cases are relatively frequent in which no definite cause can be determined. However, the more careful and thorough the examination the fewer the unexplained cases will be. It does not follow that, even though the cause is determined, the remedy is at hand. This is particularly true of the obstructive forms of sterility where either the male or the female passages are closed for the transport of the germ cells. Either one or both partners may be involved in this type of sterility. The finding of an aspermia in the male may be due to a lack of development or to an obstruction. The former may be susceptible to remedy or may be incurable, depending upon the cause. The latter may be remedied by a delicate and not too successful operation for anastomosis. It is difficult to determine in the female whether or not ova are formed, but usually the condition of the passages can be diagnosed by various tubal patency tests. If the tubes are occluded there are various types of operations, usually unsuccessful, which may be done in properly selected cases upon the insistence of the patient.

When the male is proved sterile, but his wife is not, the question of artificial insemination may arise. At present the ethical and legal status is not clearly defined. It is usually the wife who takes the initiative in the attempt to discover why she is barren. Most husbands are willing to cooperate by submitting to an examination, but some are not. Of course, there are some women do not desire to bear children.

Sometimes the history will disclose the probable cause of the female sterility and such facts as pertain to general health, evidence of disordered endocrinal or metabolic functions as of the thyroid, symptoms indicative of genitourinary disease should be ascertained. Habits of life, especially of sexual life, are important. What effect

perversions and long continued use of contraceptive methods may have on reproductive power is not known. It seems that too frequent indulgence may reduce fertility, especially in the male, and that sedentary, inactive physical life with increased weight, etc., may be a factor. The diet may be of importance and dearth of certain minerals, vitamins, etc., may be responsible for an inability to procreate.

Many of these facts can be gleaned from the history, but a careful physical examination with the necessary laboratory tests should be done. Just what these should be varies with the individual patient. There should be a general physical examination by which some pertinent facts may be discovered and also the fitness of the woman to bear children be determined. The obstetric and gynecologic features of the examination should be carried out in detail. A Hühner test should be done to determine the presence and potency of the sperm cells and, if possible, to see whether or not the genital secretions are harmful to them. It is rarely necessary to inseminate the wife artificially with her husband's semen.

The husband should be examined physically and his seminal discharge studied for presence or absence of sperms, their motility, form, maturity, etc. The presence of adventitious cells should be noted. Blood and pus cells are at times found. Impotency may be present. Neurologic diseases in either or both partners have to be discovered as they may have a bearing on the solution of the problem. The determination of the basal rates of the woman should be routinely done and any evidence pointing to a deficiency on the part of her husband should be proved by a basal metabolic test on him. Endocrinal assay and its significance is not sufficiently well established in accuracy or in experience to justify the setting forth of any positive statements. It is probable that ways and means of stimulating normal ovulation and spermatogenesis may be perfected. The timing is important, as most of the evidence indicates that the life of the ovum

is short and that the spermatozoa do not survive long in the female genital tract. Ovulation is at its peak between the ninth and fifteenth postmenstrual day. This is subject to great variation in different individuals and even in the same woman at different times and under varying conditions.

The possibility of estimating the time of ovulation in a woman by delicate electro-metric methods is a real one. Such a procedure would be of value in determining whether or not a patient ovulates and if so how often and at what period of the cycle.

#### SUMMARY AND CONCLUSIONS

This survey gives a general idea of some of the problems involved in the many aspects of preconceptional care. Fundamentally it involves the education of the physician to its importance and to its application and of lay groups as to its desirability and to its value to them and to society. It will be difficult to force the matter by law unless it is backed by popular opinion. This is evidenced by the fact that many couples migrate from districts imposing legal restrictions and are married in areas not subject to premarital laws. In some states having these laws the marriage rate has declined. The purpose back of the law is good, but the people must realize its value. The law is justified by the importance of preventing the spread of communicable disease by marriage. There are, however, many other very important aspects which laws could not now, or possibly ever, encompass even if the passage of such far reaching legislative regimentation were desirable. Education to the importance and value of preconceptional care will suffice for those who have sufficient intelligence to comprehend its significance for them and for society. For unintelligent and recalcitrant individuals other methods than educational will doubtless become effective. Again, the medical profession is called upon to recognize and to lead in the educational and technical sides of this program designed for human health and welfare.

# RELATION OF VENEREAL DISEASE TO OBSTETRICS\*

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**S**YPHILIS and gonorrhea are the two leading characters in the drama of venereal disease in association with pregnancy, the former because of its villainous nature and the latter because of its treacherous behavior. The three other venereal diseases, chancroid, granuloma inguinale, and lymphogranuloma venereum are distinctly less serious because of their actual infrequency, their usual and likely conspicuousness, and the relative safety for the fetus.

Particular points of interest are: the alteration in the course of the disease because of a pregnant state; the effect the disease has upon the product of conception; and the complications in labor and the puerperium. Since the behavior of each of the venereal diseases may be as unpredictable as a malcontent, separate discussions ensue for each clinical entity. Actually one might consider the effect of these diseases upon sterility, abortions, stillbirths, intra-uterine infections, arthritis, endocarditis, central nervous system diseases, dystocia, conjunctivitis, puerperal infection, etc., in detail. However, the present diagnostic methods, prophylactic measures, and efficient and sane therapies can stand review in light of the inadequate obstetric care that many patients still receive in the United States. Certainly part of this responsibility lies with the patient for lack of coöperation with her obstetrician, but more likely this reflects the failure of the physician and especially the obstetric leaders in those communities to "educate" the laity to the virtue and value of proper, adequate and intelligent preconceptional, prenatal, natal and postnatal care.

## SYPHILIS

Syphilis, a deceitful tricky disease, is the most important of the venereal diseases in association with pregnancy. It is sneaking and tricky because after the secondary stage is over the latent third stage may pass quietly and without symptoms. Many a syphilitic pregnant woman has had still-born or living luetic babies before any obvious clinical evidence appeared. Parran<sup>1</sup> estimates that 60,000 congenitally syphilitic children are born annually. The actual number of syphilitic mothers giving birth to nonsyphilitic babies yearly due to adequate therapy during the pregnancy is problematic. Surely the number is large.

The etiologic agent and means of spread are well established. Diagnostic serologic methods are available to all practitioners, but unfortunately not all of the profession make use of these tests in each pregnancy and as early as possible in the course of the pregnancy.

The ideal practice of premarital tests for venereal diseases, especially syphilis and gonorrhea, cannot be overstressed, as it makes possible proper therapy before conception. If every pregnant woman came under the care of her physician early in the first trimester and every physician excluded then the possibility of venereal disease in the patient, congenital syphilis could be almost completely eradicated.

Usilton, Hunter, and Vonderlehr<sup>2</sup> found that in one-half of the women syphilis was undetected before the fifth month of pregnancy. At this same time nonsyphilitic women had a stillbirth rate of 2 per cent while syphilitic women had 10 per cent

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incidence. With treatment this latter rate declined to 5 per cent.

Leading obstetricians and syphilologists agree with McCord,<sup>3</sup> and Beck and Daily<sup>4</sup> that every pregnant syphilitic woman should have adequate and active anti-syphilitic treatment throughout pregnancy. McCord, in a series of over 3,000 syphilitic gravid women, found that without treatment 35 per cent of pregnancies ended with a healthy living baby, while with treatment 95 per cent of the gestations terminated in healthy uninfected babies. He elaborates further that in every syphilitic baby there should be placental syphilis even though it is not demonstrable. It is generally accepted that transmission to the fetus takes place probably sometime after the placenta is well developed. If this correct, then treatment started by the end of the first trimester should offer the unborn child a good protection. Treatment should be begun whenever the diagnosis is made even though it is late in pregnancy. This is justified because there is a possibility that the fetus has not yet become infected (probably infrequent) and also to institute treatment for the fetus if it is diseased.

Cord Wassermanns may be negative in 37 per cent of syphilitic infants according to Cooke and Jeans.<sup>5</sup> Positive cord Wassermanns are more significant but may be misleading. Every infant of a syphilitic mother should have careful pediatric study to exclude or establish the diagnosis of congenital syphilis and should be followed for years. X-ray examination of the long bones for typical lesions should be a routine.

Another reason for administering therapy during pregnancy is that the maternal disease responds well at that time. It is true that rarely a complication contraindicates therapy, yet when it does, the situation must be carefully studied. Definite and severe kidney lesions may be one reason but not necessarily so. An occasional patient reacts unfavorably to arsenicals or is unable to tolerate the therapy. With careful management of each case, intoler-

ance and complications are less likely to occur. Plass and Wood<sup>6</sup> report that "Pregnant women are more susceptible to the deleterious as well as the beneficial effect of antisyphilitic therapy by modern arsenicals." Due to this susceptibility most syphilologists adjust the dosage and alter the routine of therapy somewhat to fit into the pregnant state. Syphilitic therapy should not be administered until a positive diagnosis has been made.

The typical primary genital lesion of syphilis has a diameter of a few to several millimeters, a necrotic-like membrane on the cup or saucer-shaped ulceration, an encircling leathery or semicartilaginous induration, little or limited hyperemia, and practically no tenderness. The secondary stage is associated with multiple lesions on the skin turning copper-like on fading, and mucous patches in the oral cavity. The spirochete of syphilis may be observed in the serum from the primary or secondary lesions by means of dark field illumination. Since the third stage is a silent period (one without symptoms and quite often without clinical findings) the diagnosis must be made through the use of serologic tests done in certified and approved laboratories. Condylomata with a flat topped wide base on the genitalia suggest that syphilitic infection exists or has existed. Impaired knee and pupillary reflexes give indication of nervous system syphilis.

Every pregnant woman should have serologic blood specimens taken on the first visit. Most places use 10 c.c. more or less for blood Wassermann and Kahn or other serologic tests. After the completion of the general history, physical and obstetric examination and routine laboratory tests the patient should return in one week for further advice and possible "check." If the serologic tests are positive or questionably positive, a second test must be made. Becker and Muir at the University of Chicago Clinics treat every pregnant woman if she has had syphilis, even though she may be asymptomatic (regardless of the serologic reaction). At the Chicago

Lying-in Hospital therapy is begun with four weekly injections of 1 c.c. bismuth salicylate and followed with first 0.3 and then 0.45 Gm. neoarsphenamine. This is three-fourths of the regular adult dosage. This arsenical treatment is given weekly for eight weeks followed by five weeks of bismuth salicylate 1 c.c. and then continued in this rotation. These courses may overlap and a definite plan to alternate is made so that neoarsphenamine is given in the last month of the gestation. An exception is made in early syphilis when arsenical preparations are administered first.

#### GONORRHEA

It is generally assumed that gonococcal infections are of little import to pregnancy. Vonderlehr and Usilton<sup>7</sup> estimate that approximately 230,000 potential mothers in the United States acquire gonorrhea annually. No reliable data are at hand to show what percentage have gonorrhea and pregnancy combined. In the past enough babies developed gonorrheal ophthalmia from their infected mothers to cause many states to pass laws requiring prophylactic treatment to the eyes of every newborn.

Gonorrhea may cause sterility through damage or injury to the uterus, tubes, and/or ovaries. (Sterility or nonfertility is caused by many conditions other than gonorrhea.) Tucker, Trussell, and Plass<sup>8</sup> cultured gonococci from 4 per cent of pregnant clinic patients, one-half or 2 per cent of whom were asymptomatic and gave a "negative history." Such data alone indicate the need for more careful scrutiny in pregnancy for gonococcal infections. As pregnancy advances, and especially with local treatment, the lower genital tract may become normal in appearance and smears become negative for the gonococcus. Yet, an acute exacerbation may take place in the early puerperium.

After the first trimester of pregnancy, spread to the tubes is hindered because the sac of the ovum fills the entire uterine cavity. Spread to the heart, joints, and kidney may take place at any time in

pregnancy, yet such complications appear no more likely during pregnancy.

After delivery the gonococcus has an open avenue again to the tubes and the peritoneal cavity. It has been said that postpartum gonococcal peritonitis is more likely a late complication. The disease pursues a course not so different from that in the nonpregnant.

The gonococci attack the urethra and cervix readily and remain in these sites, producing congestion, edema, hyperemia, and tenderness. Healing or recovery is a gradual process. Irritation on urination subsides slowly. The mucopurulent rich creamy discharge may become replaced by various vaginal discharges, the result of secondary invaders. The typical leucorrhea in vaginal trichomoniasis is bubbly, but otherwise the same rich creamy color. The vaginal walls may show evidence of infection in gonococcal infections too. Occasionally Bartholin's glands are invaded. Smears and cultures should be made from the material within the urethra, expressed from the urethral glands by pressure on the vaginal side. Urination should not immediately precede the examination. Vaginal material in the adult is less satisfactory for smear and culture studies. It is all the more important that the cultures and smears be properly taken from the urethra, cervix and the Bartholin's glands.

Bartholin's gland abscesses occur more often in association with gonorrhea than other infections. The treatment is drainage by incision. Cyst formation is not necessarily the result of gonococcal invasion, but during pregnancy only these cysts should be removed when symptoms or increase in size justify it.

Formerly condylomata acuminata or verruca acuminata were looked upon as definite earmarks of an existing or a previous specific venereal infection, but this is now known to result from several conditions, one of which is gonococcal infection.

For the product of conception there is no risk, aside from unintentional abortion

because of an endometritis or ectopic pregnancy due to tubal damage, until the membranes rupture. At the time of delivery, however, the eyes or genital tract may become inoculated. The infant's genital tract is so infrequently infected that prophylactic measures are not prescribed. In sharp contrast, the eyes offer an unusually fertile nidus which explains the importance of proper care of the conjunctival sac of the newborn.

Whenever there is any suspicion of the infection, smears and cultures should be made. McLeod's medium or a satisfactory substitute is recommended. Adair, Hesseltine, and Hac, with Taylor and Hibbs and their associates<sup>9</sup> have used this medium successfully even in Chicago winter climate for transporting the culture by trolley or car for a few miles in aerobic state (reasonable care is used to prevent pronounced chilling).

The oxydase reaction using a 1 per cent dimethylparaphenylenediamine or tetramethylparaphenylenediamine hydrochloride facilitates in the selection of colonies in heavily mixed or contaminated plates. False positive reaction may be given by *B. coli* and *B. subtilis*. Meningococci and some of the neisseria subgroups as *catarrhalis* or *flava*, may also give the same reaction. Sugar fermentations identify these properly.

	Fermentation with Acid Formation			
	Levulose	Dextrose	Maltose	Sucrose
<i>N. gonorrhea</i>	—	A	—	—
<i>N. intracellularis</i>	—	A	A	—
<i>N. catarrhalis</i>	—	—	—	—
<i>N. sicca</i>	A	A	A	A
<i>N. flava</i>	A	A	A	—

Gonococcal cultures grow dependably in reduced oxygen tension. This may be accomplished by displacing the air with

carbon dioxide from the encased petri dishes in special containers.

Carpenter, Leahy, and Wilson<sup>10</sup> stress the value of cultures over smears. The findings at the Chicago Lying-in Hospital are in accord.

Therapy is in a transitional state. Until recently only local therapies (there are several) and increased heat (locally or generally) were in good repute for the adult. The induction of general hyperpyrexia for a few to several hours is a serious undertaking and is contraindicated in association with complications or pregnancy. Local hyperpyrexia is of questionable merit particularly at present.

For a few years estrogenic hormone was employed generally for vulvovaginitis of the immature female.

Sulfanilamide therapy has replaced the other therapy but still fails to cure all. Most workers advise 60 gr. daily (15 gr. doses at four hour intervals) for five to seven days, then gradually decreasing to 45 gr. (four divided doses at four-hour intervals, 10-10-10-15 gr. each) for two weeks or longer. The patient must be observed frequently for drug reaction or intolerance (agranulocytosis, anemia, dermatitis, fever). Sulfapyridine has been recommended by some workers. A total of 45 gr. daily (15-7½-7½-15 gr.) at four hour intervals for two days, with a decrease to 30 gr. (7½-7½-7½-7½) at four hour intervals for five days. These patients must be observed carefully also.

#### CHANCROID

Chancroid infection is a localized disease, almost always found on the genitalia and caused by the Ducrey bacillus (*Haemophilus ducrey*). It produces as a rule a less indurated, or soft chancre. Inguinal lymphadenopathy is common, and one or more glands may suppurate. The various reports do not mention pregnancy in conjunction with this clinical entity. Hence there must be a relatively or actually insignificant occurrence in association with the gravid and parturient states. In the first place, chan-

croid is not a common condition and in the second place, there is rarely, if any, residual damage which might cause dystocia or be associated with other complications of parturition. Thirdly, this disease is a local process and runs a self-limited course. Thus there is slight chance of fetal or newborn infection. Whether the course of the disease is altered by the pregnant state or responds differently under this condition to therapy is unanswered. The only prophylactic measure for the fetus would be the usual cleansing at birth and the application of a non-irritating skin antiseptic. Perhaps ammoniated mercury ointment might serve the purpose.

The diagnosis may be made by finding the Ducrey bacillus (*Haemophilus ducrey*) with Gram's stains in scrapings from the primary lesion and in aspirated pus from the buboes. This organism, a streptobacillus type, may grow in defibrinated blood infusion agar (Torpin and Dienst<sup>11</sup>). Cole and Levin's<sup>12</sup> inability successfully to culture the organism justifies their stress on the specificity and value of the intradermal test. A foreign preparation (Dmelcos vaccine) or mixture of killed organisms and serum containing antibodies (which is barred from the United States) gives dependable results diagnostically. The positive intradermal test causes an infiltrated papule from 0.5 to 1. cm. in diameter in twenty-four to seventy-two hours. The induration is distinctly larger and the lesion may terminate in necrosis.

Sanderson, Greenblatt and Baethke<sup>13</sup> found the complement fixation test unreliable because of false positive reactions.

Since the reaction may persist for thirty or more years (Cole and Levin) a positive test does not prove conclusively that the lesion in question is necessarily chancroid.

Without specific reports or observations it seems that neither pregnancy nor chancroid alters the other's course. Apparently the fetus is not especially endangered and apparently therapy would not be contraindicated in pregnancy or the puerperium. Secondary bacterial invasion in

draining sinuses must be a serious complication during parturition and the early puerperium.

Therapy consists of local hygienic measures and repeated aspiration of suppurating buboes to prevent rupture and thereby avoid chronic sinuses. Secondary bacterial infection will follow surely surgical drainage which often results in chronic extensive ulceration. Torpin and Dienst mention that "frequent intradermal tests," 0.1 c.c. vaccine, may prove valuable. If draining sinuses develop, frequent irrigation or possibly injection with mild cauterizing fluids or Menciére mixture may be used. Formalin, phenol and other caustic agents have fallen into discard.

#### GRANULOMA INGUINALE

Certain proponents claim that granuloma inguinale is an infection caused by Donovan bodies or bacilli while others feel that these uncultured organisms are not true bacteria, but possibly artifacts, and further suggest that a virus is the responsible agent. The disease is essentially a local process and extends by direct spread. Lesions are usually vulvar and inguinal, but may involve the anus, the vagina, the cervix and even extragenital organs.

The majority of reports fail to discuss any significance or importance of this clinical state in relation to pregnancy, labor or the puerperium. Its general infrequency destines only a rare occurrence with pregnancy. Yet this rarity does not pardon ignorance or neglect of such possibilities.

Torpin and Dienst<sup>11</sup> recommend Wright's stain for smears presumably containing Donovan bodies. Pund and Greenblatt<sup>14</sup> observed in tissue sections an affinity by the Donovan bacilli for silver salts. Hematoxylin and eosin have been used in biopsy material by some with fair success.

The lesion is usually elevated, meaty, reddish and somewhat resembles granulomatous tissue. It is a superficial skin lesion. It is hypertrophic in nature and may become secondarily infected, thus associated with putrid or other foul odors.

Antimony and potassium tartrate (tartar emetic) and also foudadin (fuadin) are specific therapeutic agents. Antimony potassium tartrate is dissolved in saline solution and given intravenously daily or on alternate days. The first dosage is 0.04 Gm. and is increased with each treatment by .01 Gm. until 0.1 Gm. is reached. The medication is continued until the patient is clinically cured except in the event of intolerance. Rheumatoid pains are the most likely symptom of intolerance. Prompt and immediate clinical response should be anticipated.

Williamson, Anderson, Kimbrough, and Dodson<sup>15</sup> endorse foudadin and prescribe it intramuscularly in 7 per cent solution, giving 1.5 c.c. the first day, 3.5 c.c. the second, 5 c.c. the third and 5 c.c. on alternate days for six more doses, or a total of 40 c.c. in fifteen days. It seems to cause less reaction, yet it is more costly than potassium and antimony tartrate.

Scarring may follow in the wake of the receding granulomatous tissue and conceivably might thereby predispose to dystocia. An unestablished argument has been advanced that the disease, especially when involving the vagina and cervix, should spread more rapidly during the gravid state because of the succulence and vascularity of the tissues.

Thus far reports do not reveal the transmission to the fetus in utero, but surely there is a fair possibility of contamination during birth. Accordingly such exposed babies need careful observation. Perhaps proper cleansing at birth and the application of a mild antiseptic as ammoniated mercury ointment to the delicate sensitive skin might offer some means of prophylaxis.

#### LYMPHOGRANULOMA VENEREUM

The virus disease lymphogranuloma venereum is found ordinarily in adults and rather rarely in pregnant patients. Although it usually manifests itself distinctly and often extensively locally, von Haam and D'Aunoy<sup>16</sup> point out that it is a

systemic disease. Encephalitis is one of the remote infections as evidenced by the "symptoms of fever and headaches," and by recovery of the virus from the spinal fluid. The virus is transmitted by genital contact and seems to occur ordinarily in unhygienic and poor patients.

Characteristically in the female the lymphadenitis extends from the primary lesion, a papule, ulceration, or macule, which develops and vanishes, usually unnoticed by the patient, to the perirectal lymphatic structure. The femoral and inguinal glands are sometimes involved. Unless the inflammatory process is quite extensive the internal genitalia remain free. Accordingly, fertility on this basis remains unimpaired, and several observations confirm this conviction. Very excessive tissue reaction ends in complete obstruction of the rectum (necessitating colostomy) and often the elimination of all space in the pelvis by a firm inelastic inflammatory tissue. In extreme states necrosis may involve any of the pelvic structures, more likely the vagina, rectum, rectovaginal septum, ischio-rectal fossa, and/or much of the lower pelvis.

After the reaction reaches a given point (varying extremely in patients) it remains stationary for an uncertain period, after which an involution, incomplete to a variable degree, follows. With sufficient involution some physiologic functions, such as normal bowel action, are reestablished. After this a colostomy wound may be closed. Inasmuch as the Frei test remains positive for years after the original infection, it is necessary that the clinical findings confirm the diagnosis. The intradermal injection of 0.1 c.c. antigen (attenuated human pus or mouse brain) should produce a papule 7 mm. or more in diameter with a wider induration and hyperemia for a typical positive reaction.

Human source varies in its concentration; yet Binkley and Love<sup>17</sup> find it more reliable than mouse brain antigen. Grace and Suskind,<sup>18</sup> however, advocate mouse brain antigen. So far, it is the only available



commercial source and is uniform in its potency. When the mouse antigen is used, a control of non-infected mouse brain emulsion should be employed. Careful observations, after the twenty-fourth hour and up to the seventy-second hour will almost exclude false positive and false negative evaluations.

A specific and efficient agent would be a therapeutic boon. Perhaps more favorable response has occurred with the use of the Frei antigen of human source than other agents, unless sulfanilamide, now under investigation, should prove effective. The mouse antigen has not been used therapeutically. Human pus is diluted from 1 to 4 to 1 to 10 with saline solution and the virus killed by exposure to 60°C. temperature for two hours on two successive days. Torpin, Greenblatt, Pund and Sanderson<sup>19</sup> state that the intravenous route has not been shown to be more effective. The intravenous dosage starts with 0.05 c.c. and is increased gradually to 0.3 c.c. Intramuscular doses begin with 0.1 c.c. and increase to 2 c.c. This therapy is continued until the condition improves or fails to respond. Shropshear,<sup>20</sup> Knight and David,<sup>21</sup> Shaffer and Arnold,<sup>22</sup> Marino, Turell, Buda and Nerb<sup>23</sup> announce a moderate to a good improvement after sulfanilamide administration. In the absence of concrete data moderate amounts only of sulfanilamide should be tried until more information is available on the optimum dosage. Moreover, not all cases have been cured by this drug.

The few observations made during pregnancy indicate an unaltered effect upon the disease process. The disease may, on the other hand, alter appreciably the course of labor through dystocia from serious or impossible obstruction to the birth canal. Special managements have been used in some cases at the Provident Hospital (Chicago) because of pelvic obstruction (Wilson and Hesseltine<sup>24</sup>). The tragedies of Anderson,<sup>25</sup> Vignes,<sup>26</sup> and Gaines and McDowell<sup>27</sup> illustrate this point more emphatically. Fortunately, the combina-

tion of pregnancy and lymphogranuloma venereum is infrequent.

Sterility may result if there is injury to the uterine cavity, tubes, or ovaries, yet conception occurred in a patient after colostomy to relieve bowel obstruction.

Tests by Dich<sup>28</sup> and Babonneix, Fouraine and Lafont<sup>29</sup> revealed positive reactions in children. Yet of the entire group only one case report suggests congenital transmission. This baby had a positive Frei reaction on the fourteenth day of life, but it was without clinical manifestations.

Wilson and Hesseltine<sup>24</sup> found only one positive reaction in several children born of mothers with typical clinical lesions and typical reactions to intradermal Frei antigen.

All babies whose mothers have lymphogranuloma venereum should be observed and tested over a prolonged period for this disease.

#### GENERAL DISCUSSION AND CONCLUSION

Since extragenital lesions of the various venereal diseases have been reported and well proved, one may well anticipate such possibilities for the baby, due to inoculation as it traverses the infected birth canal. Syphilis may be acquired from a primary genital sore. Gonococci may find their way to a favorable nidus in the newly born child through contamination at birth. Certainly, chancroid, granuloma inguinale and lymphogranuloma venereum must present such risks at the natal period.

Gonorrhea is a major problem because of the possibility of spread to the maternal internal genitals and the peritoneal cavity in the postpartum period, and also because gonorrheal conjunctivitis in the infant occurs even in spite of prophylactic measures, not to mention the infrequent genital infections in the infant.

Syphilis is the scourge of the lot, for most pregnant women with this disease are without symptoms and usually without clinical findings. Every effort must be ventured to eradicate congenital syphilis. Although new mercurial, bismuth, and arsenical prepara-

tions are offered to the profession from time to time as more efficient and safer, their use during gestation must be postponed until enough investigation has been made to prove their value. Castello and his associates<sup>30</sup> and Goldberg<sup>31</sup> state that neoarsphenamine is the most dependable arsenical available from the viewpoint of the fetus. McCord uses mercury in place of bismuth as it is without pain and avoids frightening the patient by use of a needle.

The incidence of syphilis varies in different communities and in different groups of the same area. It is found in about 1 per cent of the Chicago Lying-in Hospital patients.

Every genital sore or lesion during pregnancy should be investigated. All discharges should be examined. Smears and cultures from the cervix and urethra are indicated if there is any question of infection of these regions. The smear should be stained by Gram's method (gentian violet followed by Gram's iodine, destained and then counterstained with safranin). Cultures are practical, but only in centers able to prepare fresh mediums and where the cultures may be immediately and properly incubated.

Every woman in every pregnancy should have a serologic (Wassermann, Kahn, or other) test at the first visit. Prevention of congenital syphilis is the only justifiable therapy. Patients must be "educated" to the value and benefit of adequate and intelligent prenatal care beginning in the first trimester. Every physician should make adequate serologic tests to exclude syphilis in every gravid patient in every pregnancy and treat actively each case of syphilis throughout the pregnancy if he is to practice the best obstetric medicine. This is rendering the best possible service to the mother and to the unborn child.

#### REFERENCES

- PARRAN, T. Control of syphilis. *J. A. M. A.*, 109: 205, 1937.
- USILTON, L. J., HUNTER, H., and VONDERLEHR, R. A. Prevalence, incidence, and trend of syphilis in Chicago. *J. A. M. A.*, 110: 864, 1938.
- MCCORD, J. R. Syphilis in pregnancy. *Surg., Gynec., & Obst.*, 66: 441, 1938.
- BECK, A. C., and DAILY, W. T. Syphilis and pregnancy. *Am. A. Adv. Science*, 6: 101.
- COOKE, J. V., and JEANS, P. C. Transmission of syphilis to the second generation. *Am. J. Syph., Gonorr. & Ven. Dis.*, 6: 569, 1922.
- PLASS, E. D., and WOODS, E. B. Hemorrhagic encephalitis (neoarsphenamine) in obstetric patients. *Am. J. Obst. & Gynec.*, 29: 509, 1935.
- VONDERLEHR, R. A., and USILTON, L. J. Gonorrhea problem in the United States. *J. A. M. A.*, 109: 1425, 1937.
- TUCKER, W. W., TRUSSELL, R. E., and PLASS, E. D. Latent gonorrhea in obstetric patients. *Am. J. Obst. & Gynec.*, 38: 1055, 1939.
- ADAIR, F. L., HESSELTINE, H. C., HAC, TAYLOR, and HIBBS. Unpublished data.
- CARPENTER, C. M., LEAHY, A. D., and WILCOX, K. M. A comparison of the results of the smear and cultural methods for the diagnosis of gonococcal infections in adult females. *Am. J. Syph., Gonorr. & Ven. Dis.*, 22: 55, 1938.
- TORPIN, R., and DIENST, R. B. Chancroid infection in the female. *Am. J. Syph., Gonorr. & Ven. Dis.*, 22: 634, 1938.
- COLE, H. N., and LEVIN, E. A. Intradermal reaction for chancroids with chancroidal pus. *J. A. M. A.*, 105: 2040, 1935.
- SANDERSON, E. S., GREENBLATT, R. B., and BAETHKE, E. Complement fixation test in chancroid infection. *J. Lab. & Clin. Med.*, 24: 185, 1938.
- PUND, E. R., and GREENBLATT, R. B. Granuloma venereum of cervix uteri (granuloma inguinale) simulating carcinoma. *J. A. M. A.*, 108: 1401, 1937.
- WILLIAMSON, T. V., ANDERSON, J. W., KIMBROUGH, R., and DODSON, A. E. Specific effect of "fouadin" (fuadin) on granuloma inguinale. *J. A. M. A.*, 100: 1671, 1933.
- VON HAAM, E., and D'AUNOY, R. Infectivity of the spinal fluid in lymphogranuloma inguinale. *J. A. M. A.*, 106: 1642, 1936.
- BINKLEY, G. W., and LOVE, P. R. Mouse brain lymphogranuloma venereum antigen. *Arch. Dermat. & Syph.*, 38: 383, 1938.
- GRACE, A. W., and SUSKIND, F. H. Use of standard mouse brain antigen. *J. A. M. A.*, 107: 1359, 1936.
- TORPIN, R., GREENBLATT, R. B., PUND, E. R., and SANDERSON, E. S. Lymphogranuloma venereum in the female. *Am. J. Surg.*, 43: 688, 1939.
- SHROPSHEAR, G. Sulfanilamide in the treatment of stricture of the rectum caused by lymphogranuloma venereum. *Illinois M. J.*, 74: 153, 1938.
- KNIGHT, A. A., and DAVID, V. C. Treatment of venereal lymphogranuloma with sulfanilamide. *J. A. M. A.*, 112: 527, 1939.
- SHAFFER, L. W., and ARNOLD, E. Lymphogranuloma venereum, especially its treatment with sulfanilamide. *Arch. Dermat. & Syph.*, 38: 705, 1938.
- MARINO, A. W., TURELL, R., BUDA, A. M., and NERB, L. Treatment of venereal lympho-

- granuloma with sulfanilamide. *Am. J. Surg.*, 46: 343, 1939.
24. WILSON, C. L., and HESSELTINE, H. C. Unpublished data.
  25. ANDERSON, R. E. Rectal stricture complicating labor. *Memphis M. J.*, 13: 184, 1938.
  26. VIGNES, H. La maladie de Nicolas-Favre en gynécologie et en obstétrique. *Rev. franç. de gynéc. et d'obst.*, 34: 215, 1939.
  27. GAINES, C. D., and McDOWELL, J. F. Rectal stricture complicating delivery; report of a fatal case. *J. A. M. A.*, 107: 964, 1936.
  28. DICH, W. Ist das Lymphogranuloma Inguinale auf die Nachkommenschaft über Bragbar. *Med. Klin.*, 32: 319, 1936.
  29. BABONNEIX, L., TOURAINE and LAFONT. Valeur de la réaction de Frei; cent réactions de contrôle chez l'enfant. *Bull. Soc. franç. de dermat. et syph.*, 42: 767, 1935.
  30. CASTELLO, M. A., COPPOLINO, J. A., RAKOFF, A. E., ROEDER, P. H., and DICKSON, G. S. Mapharsen in the treatment of syphilis complicating pregnancy. *Am. J. Syph., Gonorr. & Ven. Dis.*, 23: 332, 1939.
  31. GOLDBERG, M. Mapharsen as a substitute for neoarsphenamine in agranulocytic angina following neoarsphenamine therapy in a pregnant syphilitic woman. *Am. J. Syph., Gonorr. & Ven. Dis.*, 23: 79, 1939.



WHILE we still have destructive wars, famine and pestilence are not now the important factors in depopulation in most civilized countries. . . . The voluntary restriction of reproduction caused by the practice of contraception and the induction of abortion has much more effect on the equalization of birth and death rates than did the excessive mortality in the presence of unlimited propagation.

From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

# RELATION OF TUBERCULOSIS TO OBSTETRICS

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SINCE tuberculosis is conceded to be a serious problem among girls and young women and since its incidence in this group is not diminishing as rapidly as in other age and sex groups of the general population, the association of tuberculosis and childbirth continues to be an important problem in preventive medicine. Edna E. Nicholson of the National Tuberculosis Association, in her study of tuberculosis among young women, states: "We know this phenomenon [i.e., the relative high death rate among girls and young women] has existed in the United States at least since 1900, and in view of the fact that mortality figures of England, Wales and Ireland show the same deviation as far back as 1860, it seems reasonable to suppose that for one reason or another, young women have always been more prone to die of tuberculosis than have their young brothers or older sisters."

Notwithstanding the tremendous amount of very excellent educational and preventive work accomplished during the past thirty years, tuberculosis is still responsible for some 60,000 deaths annually in the United States. Of this number about 29,000 are females and approximately 18,000 of these are between the ages of 15 and 45 years. Just what proportion of this latter group became pregnant and aborted or had premature labor or gave birth at term is not known. There are no available statistics with which to answer this question. We do know however that, as a general rule, the gravida who has tuberculosis does not receive adequate care during pregnancy, labor, the puerperium and for a sufficient period of time following these events properly to "cure" active tuberculosis or keep quiescent tuberculosis "arrested."

Neither does she always receive adequate obstetric attention. We know also that one of the main reasons for this state of affairs has been the woeful lack of coöperation between accoucheur and phthisiologist, stimulated by the almost complete absence of proper hospital and sanatorium facilities. Thus we may well account for much of the confusion that exists as to the effect of pregnancy, parturition and the puerperium and their end-results upon tuberculosis.

For the past few years, however, this gap has been slowly "closing in" because medicine has gotten to a stage in its evolution where no sane physician believes himself competent to practice medicine without help from his colleagues who, although they may not be classed as specialists, have superior knowledge in one field or another. No modern obstetrician or physician doing obstetrics therefore should attempt to handle a case of pregnancy associated with tuberculosis without the diagnosis, advice and full coöperation of an internist with knowledge of tuberculosis, or better still a phthisiologist or tuberculosis specialist. Furthermore, in view of the more recent improvements in case finding technique, in diagnosis and treatment of tuberculosis and in the management of pregnancy (prenatal care), labor, delivery and the puerperium, we should "now and here" cease quoting the statements and statistics put out by perfectly sincere authors of ten to twenty years ago. Such statistics are obsolete and are a detriment to an up to date understanding of this most important problem.

In still further substantiation of these statements, regarding lack of interest, coöperation and facilities among interested

groups, Alice M. Hill\* called attention to the appalling fact that only eighty-seven, or 21 per cent, of 413 out of a total of 463 (413) that admit or retain pregnant women and take care of them through delivery; 247 or 60 per cent of the 413 sanatoria

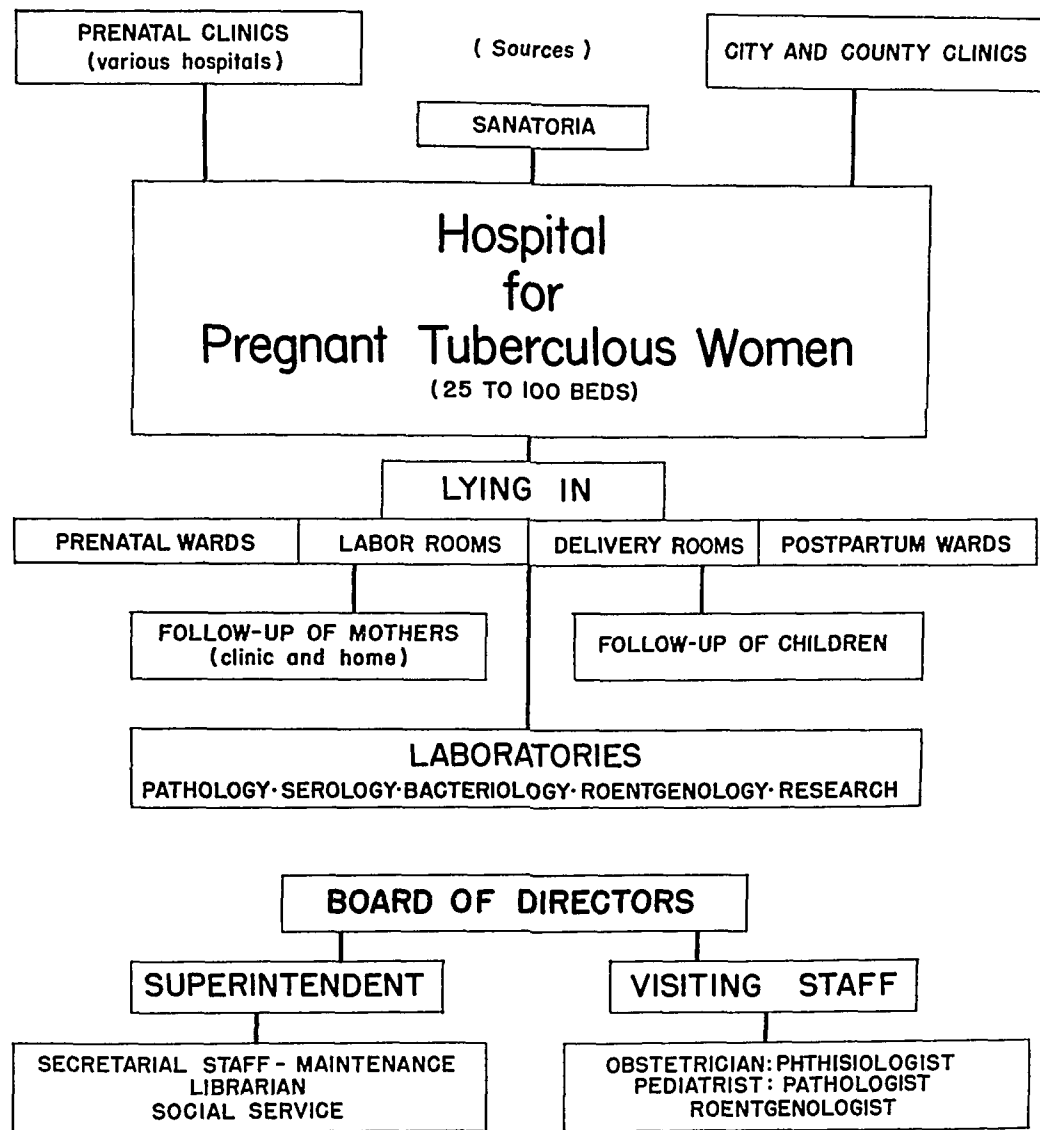


FIG. 1. Set-up of institution devoted entirely to care of pregnant tuberculous women. The ideal arrangement.

sanatoria in the United States, admit and retain pregnant tuberculous women and keep them through delivery. Of these institutions forty-three are general hospitals, thus leaving only forty-four tuberculosis sanatoria, or 10.6 per cent of the total

\* While these figures were published in 1927 there is no reason to believe that conditions are materially different today. This is the unanimous opinion of two internationally known tuberculosis statisticians, who prefer to remain anonymous.

admit pregnant women but transfer them to general or special hospitals or to their homes for the delivery. Furthermore, we find that 24 per cent of the private sanatoria do not admit pregnant women at all, and only 17 per cent of them keep the patient through delivery. Of the state sanatoria only 10 per cent keep their pregnant patients through delivery, while 71 per cent admit them before time for the

delivery. Of the county sanatoria 22 per cent keep them through delivery, and 65 per cent transfer them for delivery.

city of New York is not in much better position for there are only two or three institutions in the city where the tubercu-

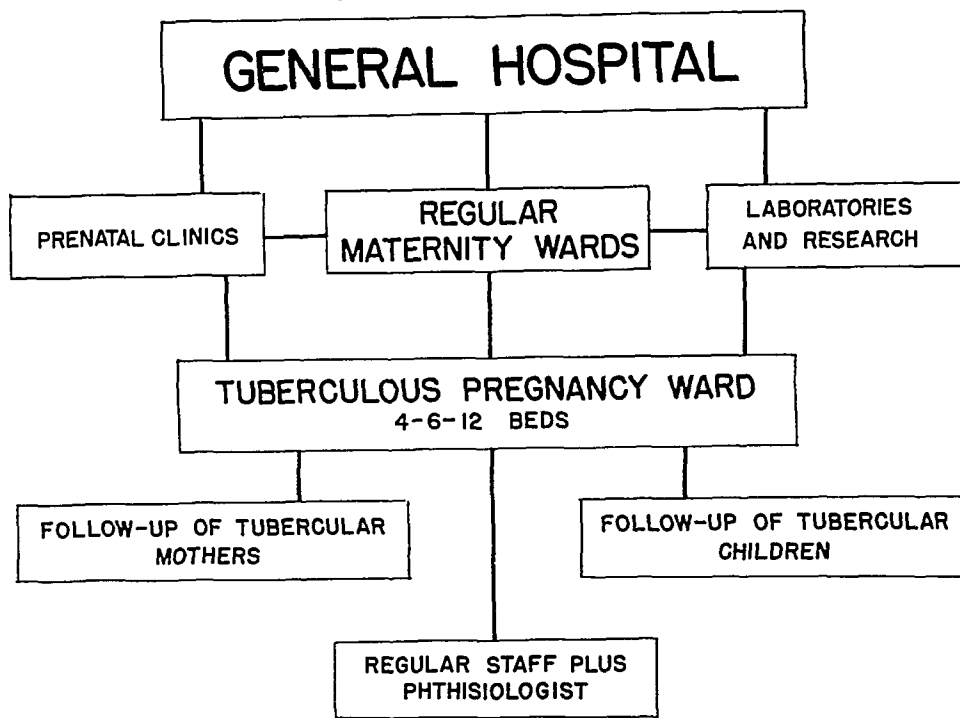


FIG. 2. Alternative arrangement of wards for pregnant tuberculous women in a general hospital.

In this report by Dr. Hill, nothing was said about the adequacy of the care these patients receive. Nevertheless, from the standpoint of their tuberculosis, there can be little doubt as to the adequacy of the treatment; from the standpoint of the pregnancy, labor and puerperium there is grave doubt. This is a natural supposition, for no one would expect an expert obstetrician interested in tuberculosis to be associated with a tuberculosis sanatorium, except perhaps those few situated in or near the larger cities. Conversely, it would not be expected that the phthisiologists of these institutions would be good obstetricians. Of the eighty-seven sanatoria reporting facilities for the care of pregnant tuberculous women, only a very few, probably not over ten to twelve, actually carried out the proper management of the pregnancy, the labor and the puerperium. The vast majority did the best they could with the facilities they possessed, realizing full well their inadequacies. The greater

lous woman who is pregnant can be adequately cared for through delivery and beyond the lying-in period for as long as is necessary to render her safe to return home.

What then is to be done to insure adequate care, both medical and obstetric, for the pregnant tuberculous woman? The following plan is suggested:

1. The ideal set-up for the adequate management of tuberculosis and pregnancy would be a special institution devoted exclusively to the care and treatment of pregnant tuberculous women. Here would be working in close harmonious coöperation a specialist in tuberculosis; an expert obstetrician interested in tuberculosis; a pediatrician also interested in tuberculosis; a roentgenologist; and the whole group supported by good pathologic, serologic and bacteriologic laboratories. In such an institution the tuberculosis, the pregnancy, the labor and the puerperium and the baby immediately after birth, could be adequately handled, and the "follow-up"

of mother and baby could be ascertained with accuracy. Furthermore, research in pathology, serology and bacteriology of tuberculosis, including congenital tuberculosis, could be pursued to the end that something definite and constructive might supplant the confusion and chaos now existing.

2. In lieu of this ideal set-up the following is proposed, viz., that each hospital group interested be allocated a certain number of beds for pregnant women with tuberculosis and that these patients be under the direct supervision of a tuberculosis specialist in coöperation with an obstetric specialist who is interested in tuberculosis. After the seventh month of the pregnancy the obstetrician should assume first control of the patient with the tuberculosis specialist coöperating, the obstetrician to continue in charge until after the postpartum period (two or three weeks or longer), following which the tuberculosis specialist again assumes charge and manages the case as he would any other case of tuberculosis.

The management of the baby should be put under the direct supervision of a pediatrician interested in tuberculosis as soon as the umbilical cord is ligated. Decision as to the extent of mother-baby association, if any, can thus be made before contact infection of the baby takes place. This arrangement is of the utmost importance, particularly where the mother's sputum is positive for tubercle bacilli. The pediatrician, of course, should follow the child through the adolescent period and see to it that a good internist interested in tuberculosis takes charge when he shall have finished his job.

With either of these arrangements (of course the first is the most ideal) research could be carried on by the various individuals concerned in the management of these cases and, with the coöperative teamwork of the various laboratories, reliable end-results could be ascertained. Moreover, classification, typing, diagnosis and management of the tuberculosis would become

much more standardized than has hitherto been possible. Naturally, no plan will be successful unless the coöperating physicians—tuberculosis specialist, obstetrician, pediatrician, roentgenologist, pathologist, serologist and bacteriologist—are vitally interested in this type of work. For smaller communities where such complete coöperation is not possible, every effort should be made to obtain the services of one who knows tuberculosis. This is one situation where the various State Departments of Health or, in those states unable to coöperate, the United States Public Health Service, could render a valuable consultation service without in any way encroaching upon the rights and privileges of the private physician. Since the President has proposed a plan for government constructed hospitals in communities where there is need but not the finances, some of this construction could be carried out to provide improved facilities for the care of pregnant women who have tuberculosis. No better way of spending public funds, it seems to me, could possibly be found.

#### EFFECTS OF PREGNANCY ON TUBERCULOSIS

At the outset of any discussion of the effects of pregnancy upon tuberculosis we should have clear in the "mind's eye" that it is not pregnancy alone that is meant but the entire cycle of events implicated in childbirth—gestation, labor, delivery and the puerperium.

It should be constantly kept in mind that the type or character of the tuberculous lesion is far more important than the extent of the disease. Merely the designation of whether a given lesion is minimal, moderately advanced, or far advanced is not nearly so important, although, of course, it is quite necessary, as the pathologic character of the lesion. Experience, during the past decade has impressed upon the phthisiologist the fact that in the exudative or pneumonic types of the disease the prognosis is not nearly so favorable as in the productive or fibrous types. This knowledge becomes of more value in

relation to tuberculosis and pregnancy when we bear in mind that the more destructive and fatal types of tuberculosis (exudative or pneumonic) occur more frequently in the younger age and sex groups, particularly in young females, whereas the less destructive types (productive or fibrous) occur more frequently in those past middle life. In other words, during the most prolific reproductive period of a woman's life, she is also subject to the most devastating types of tuberculosis. Is it any wonder therefore, that before the advent of a more thorough understanding of the tuberculous process and a better coöperation between the modern phthisiologist and obstetrician, the maternal mortality rate in pregnancy, parturition and the puerperium in tuberculosis remained alarmingly high? Likewise, is it any wonder that abortion was so frequently performed?

Today the picture has changed. With the newer concepts of the pathologic type or character and clinical behavior of tuberculosis, the phthisiologists have developed improved methods of case finding, of diagnosis and of treatment. Some types require more heroic treatment than others. Whereas all types require the accepted routine "cure" treatment, including pneumothorax in a large percentage of cases, others require, in addition, the more drastic procedures of phrenicotomy or thoracoplasty. Incidentally, thoracoplasty, although requiring at least two extensive surgical operations, is not looked upon today as the mutilating procedure of doubtful value that it was a decade or more ago. Its results are indeed gratifying. Surgery has come to be another important affiliate in the treatment of tuberculosis.

Now let us ask the question—What changes, if any, in the treatment of the tuberculosis are indicated during pregnancy, labor and the puerperium? Formerly this was a much debated question; today it is certain that the pregnant woman should have identically the same treatment as her nonpregnant sister who has tuberculosis. In more recent years, collapse

therapy has been practiced extensively during pregnancy with gratifying results for the tuberculosis and apparently with no ill effects on the gestation, the labor, or the delivery. There are several reports in the recent literature on this phase of the subject. For example, Seely, Siddall and Balzer of Detroit, report in detail a study of fifty-four cases of tuberculosis and pregnancy treated with collapse therapy before and during the pregnancy, immediately after labor and during the puerperium, with uniformly good results. They had nineteen cases in which treatment was begun *before* pregnancy and 90 per cent of these were arrested or improved. In thirty-five cases treated during pregnancy, 77 per cent showed arrest or improvement, while 23 per cent were made worse and of this latter group fourteen per cent died within one year after confinement.

In a more recent report the same authors cite ten cases of pregnancy and parturition following thoracoplasty for advanced tuberculosis from the Herman Keifer Hospital of Detroit. They were also able to find twenty-one cases in the literature, making a total of thirty-one such cases for study. In this group, interestingly enough, four successful thoracoplasties were done during pregnancy. These thirty-one women gave birth to thirty-four babies, five prematurely. "One mother died and five others had serious exacerbation of the tuberculosis during pregnancy or within one year after delivery." Thus 19.3 per cent of these mothers had a reactivation of their tuberculosis, one to the extent that she died, while 80.7 per cent were not affected or at least not made worse.

Another report by Ornstein and Epstein from Sea View Hospital in New York, cites a group of eighty-two pregnant women with tuberculosis whom they delivered, in which 24.3 per cent were made worse. Of these 12.2 per cent died, thus leaving 75.7 per cent in the "stationary" or improved group. In this series there were twelve women upon whom thoracoplasty had been performed and who later became pregnant,



delivered their babies (one of these women had two children) and "not a single one of them had any appreciable reactivation of tuberculosis." Thus two geographically widely separated groups of tuberculous pregnant women, under almost ideal supervision, show comparable excellent results. When it is recalled that patients on whom thoracoplasty has been performed are far advanced cases with cavitation these reports appear little short of witchcraft to those who maintained that no woman with far advanced active or inactive tuberculosis, regardless of the type of lesion, should have a baby. Those familiar with the statistics on tuberculosis and pregnancy will see at a glance that the modern figures quoted above and obtained by coöperative teamwork, with adequate facilities, are many times better than those of ten and twenty years ago. Thus again we reiterate that the older statistics are obsolete.

It seems evident from a review of the recent literature coupled with a limited experience, that while collapse therapy is the greatest advance in treatment for the pregnant tuberculous woman to date, it does not entirely solve the problem. It still cannot be said with propriety, as some recent observers have stated, that pregnancy *has no effect* on tuberculosis. We can say, with certainty, that it does, but that with the more heroic methods in the treatment of the tuberculosis, coupled with improvement in obstetric care, and closer and more harmonious coöperation between the patient, the accoucheur and the phthisiologist, the entire problem is certainly less difficult at the present time than it has been in the past.

#### EFFECT OF TUBERCULOSIS ON PREGNANCY

The effect of tuberculosis *per se* on the course of gestation is negligible. It has no effect on fecundity; in fact in many instances where the tuberculosis is not debilitating and the "cure" is conscientiously taken, fertility seems to increase as the general health improves. The develop-

ment of the fetus is normal. Abortion or premature labor is somewhat more frequent than in the nontuberculous patient, particularly, in those cases with exhausting cough, hemoptysis, fever and marked general debility.

In the less advanced cases going to term or near term the labor may be completed without cause for alarm. In the far advanced cases labor may be tedious, prolonged and fraught with many dangers to the mother, as for example in the presence of dyspnea, cough, hemoptysis, impending cardiac failure, pulmonary edema or spontaneous pneumothorax.

Upon the puerperium, minimal or moderately advanced tuberculosis seems to have no effect; the incidence of postpartum hemorrhage is no greater and involution is generally not retarded. In the more active, extensive and progressive cases there is apt to be excessive hemorrhage and involution may be tardy.

From the accumulated evidence to date, it may be concluded that whatever deleterious influences tuberculosis has on pregnancy, parturition and the puerperium are not due to the tuberculosis *per se* but are entirely dependent upon the general status of the woman, i.e., whether she was debilitated or in good physical condition before conception, during gestation and following parturition.

Pregnancy complicating laryngeal tuberculosis is distinctly bad. According to Myerson, the incidence in females in the age group 15 to 40 years runs about parallel with that for pulmonary tuberculosis in this age group. Age is a definite influencing factor in tuberculosis of the larynx. The older the patient the less likelihood of her developing laryngeal tuberculosis. Again, therefore, we see the young woman a possible victim of a grave complicating tuberculous lesion, superimposed upon her already far advanced pulmonary tuberculosis, in the presence of pregnancy and confronted with the possible deleterious effects of labor and the puerperium. Truly a gloomy picture! We can readily agree

with Myerson and others, that pregnancy should not be contemplated in the presence of laryngeal tuberculosis.

While congenital tuberculosis is possible, as shown by Whitman and Green who have collected from the literature forty-seven authentic cases, it is relatively rare. Although constantly on the lookout, I have never seen a case, but believe if systematic study was made on every baby and placenta of a tuberculous mother, particularly in the more advanced cases, and especially the acute miliary type, more cases of congenital tuberculosis would be found than have hitherto been discovered. Furthermore, "Sitzenfrey has demonstrated in women dying of tuberculosis the presence of bacilli in the interior of ova while still within the Graafian follicles" (Williams). This could lead, although impossible to prove, to congenital tuberculosis.

#### MANAGEMENT OF PREGNANCY AND TUBERCULOSIS

The active management of pregnancy complicated by tuberculosis naturally divides itself into (1) the general and (2) the obstetric.

The general treatment of the tuberculosis is, as stated above, identical with that for the nonpregnant patient. With, however, the added "load" of pregnancy, causing an increase in metabolism, oxidation, and innervation, which in turn throws extra work upon the circulation and elimination, more intensified attention to fresh air, diet, rest and exercise must be given. Otherwise the phthisiologist, in full coöperation with the obstetrician, manages the case as he would any other patient with tuberculosis. Likewise, the obstetrician manages the pregnancy, the labor and the puerperium just as he would an obstetric patient who had any serious systemic disease. Adequate prenatal care\*—never omitting a single item that the most meticulous authorities have laid down as adequate—must be

given the gravida who has tuberculosis. If "a watchful eye can save a life when diligently and constantly focused on the object of its stare" in obstetrics or tuberculosis alone, think how very much more indispensable this becomes in the combination of pregnancy, parturition, the puerperium and tuberculosis. Intelligent, friendly and full coöperation between patient, phthisiologist and accoucheur is required if the best results are to be obtained.

The obstetric management includes (1) the question of the interruption of the pregnancy; (2) the method by which interruption is best accomplished; and (3) the best method of delivery at or near full term.

As to the question of the interruption of the pregnancy there are two valid indications: (1) the vital indication, where it is necessary to save the life of the gravida with far advanced tuberculosis who in the opinion of the phthisiologist is in immediate danger of dying; and (2) the prophylactic indication, where abortion is done after all therapeutic measures have failed to retard the progressive extension of the disease, which may be expected to be still further activated from pregnancy, labor and the puerperium. The vital indication is rarely, if ever, indicated. Today such a patient would not be allowed to become pregnant, and if by chance pregnancy did take place, interruption of the gestation would probably *not be recommended*. Abortion would be equally, if not more, hazardous than labor at or near full term, and in addition would provide no handicap to the offspring. The prophylactic indication is definitely on the wane. With the newer concepts of the pathologic and clinical behavior of the various types of lung tuberculosis and the more heroic methods in their treatment, as outlined above, therapeutic abortion is not practiced to the extent that it was in former years. This is as it should be, for as in heart disease, thyrotoxicosis, diabetes and affections of the kidneys, etc., the more accurate our knowledge has become the better we understand these serious systemic diseases

\* The reader is referred to any standard text for details on prenatal care.

and the better we are able to cope with them in the presence of pregnancy and parturition. What was formerly an indication for therapeutic abortion is not an indication today. This is particularly true of tuberculosis and pregnancy. Consequently therapeutic abortion is not considered necessary except where the tuberculosis cannot, for various reasons, be properly managed; when the tuberculous lesion is so far advanced as to preclude successful "arrest" when first seen by the obstetrician; or in the very fulminating malignant types of caseous pneumonic tuberculosis with cavitation that do not yield to collapse therapy, including thoracoplasty.

The method of choice in interrupting the pregnancy and the conduct of labor at or near term constitutes a very important phase in a pregnancy complicated by pulmonary tuberculosis. First of all, the best method whether early or late, is that method which will cause the *least trauma and shock* to the mother. Interruption during the first six to ten weeks can oftentimes be done by the use of the cervical and vaginal pack, particularly in the multiparous patient, followed by curettage under local, cyclopropane or gas-oxygen anesthesia, or in suitable cases, under obstetric analgesia without anesthesia. If the cervix is long, firm, and tightly closed, anterior vaginal hysterotomy under local, spinal, sacral, or cyclopropane or gas-oxygen anesthesia is the operation of choice. We usually induce obstetric analgesia by some one of the many methods—morphine-scopolamine, nembutal, sodium amytal, paraldehyde, etc.—before administration of the anesthesia (local or general). This proves very satisfactory for both patient and operator. We *never* use ether anesthesia unless there is no other way out. From the twelfth to sixteenth weeks, anterior hysterotomy following the above technique is the best procedure, except in those cases where the cervix is short, soft and patulous. Then rupture of the membranes, insertion of a vaginal or cervico-vaginal pack or a Voorhees bag, or both,

serves to start uterine contractions, to promote cervical dilatation and hasten uterine evacuation. Bleeding, should it occur, must be promptly controlled and shock vigorously combated. Remember that these patients are apt to be quite ill and debilitated, and hence succumb more quickly to trauma, hemorrhage, shock and sepsis than the average obstetric patient. Prevent trauma, conserve blood (De Lee) and prevent or promptly combat shock should be the motto of every obstetrician and gynecologist.

From the sixteenth to twenty-eighth week of gestation, artificial interruption should very rarely be undertaken, except in the very desperate cases where, in spite of proper treatment, the patient is rapidly growing worse. If intervention is decided upon, sufficient Roentgen ray (2000–3000 R) to cause abortion is given, or radium is inserted in doses of from 1200 to 1500 mg. hours within the pregnant uterus, using local or cyclopropane anesthesia. These doses of x-irradiation are not usually sufficient for the production of permanent castration, but do bring on an amenorrhea of from a few months to two or more years. Vaginal hysterotomy is a very efficient, quick, and easy method of evacuation of the uterus and the method we prefer unless the patient is extremely ill. In the latter case x-ray is preferable. Following the vaginal hysterotomy, when the patient has improved, sterilization, if advisable, can be accomplished by x-ray or radium. In young women where it is not deemed advisable to use x-irradiation, the oviducts can be ligated per vaginam if the patient's condition warrants at the time hysterotomy is performed, or if, as some operators prefer, abdominal hysterotomy is performed, the Fallopian tubes can be ligated very easily. Should every patient aborted be sterilized? Certainly not, for with proper medical care, it might well be possible for the tuberculosis to become "arrested" and after two or three years or more the patient could again become pregnant and, under proper care, carry to or near full term with safety.

From the twenty-eighth to fortieth week, nothing can be done that will improve conditions. The phthisiologist having gone the limit in treating the tuberculosis, watchful waiting may seem cowardly, but operative interference is almost sure to terminate fatally. However, here as elsewhere in medicine and surgery, individualization counts for a great deal. Under certain extenuating circumstances almost any established form of treatment may be altered, oftentimes with fairly good success.

If the pregnancy has been carried to or near full term the labor should be made as easy and short as possible. When labor pains are at regular and frequent intervals and the cervix is dilated to the size of a fifty-cent piece, (2 to 3 cm.) morphine-scopolamine analgesia, or some one of the many other effective and well known methods of securing obstetric analgesia, should be employed to a degree sufficient for the relief of the stress and strain of the labor. As soon as the cervix is fully dilated, rupture of the membranes, if these have not previously ruptured, episiotomy and the application of forceps and immediate delivery, using *local*, gas-oxygen or cyclopropane anesthesia during the active delivery, is the procedure of choice.

If the breech is presenting, follow the same routine, except complete the delivery of the breech as soon as possible. *Full cervical dilatation* should be present before any method of delivery is carried out. In the presence of a normal pelvis and baby, with fully dilated cervix and ruptured membranes, pituitrin,  $\frac{1}{4}$  to  $\frac{1}{2}$  c.c., may be given. This with episiotomy and gas-oxygen anesthesia, will accomplish delivery in the shortest possible time and with the least shock to the mother. Piper forceps applied to the after-coming head in these breech deliveries often saves time and trauma, both to baby and mother.

Version and breech extraction should not be performed in the presence of advanced tuberculosis, except on strictest indications, because of the deep anesthesia required, the extra trauma that is necessarily

produced and the greater chances of infection. This is particularly true in the collapse therapy cases. The obstetrician must plan the method of delivery, having obtained accurate pelvic measurements (by x-ray if possible) and estimated the size of the baby, so that version and extraction or other "shocking" operative procedures will not, as a last resort, have to be undertaken. We believe, when there is any doubt, either of the ability of the pulmonary lesion to withstand the strain of labor in a given case or where the bony pelvis and/or the child shows evidence of possibly causing dystocia, elective cesarean section or cesarean section after a short test of labor without progress is indicated.

If there is disproportion between the child and the pelvis or other cause for apprehension on the part of the obstetrician as to the outcome of the labor, elective cesarean section, at or near term, under *local* or gas-oxygen or cyclopropane anesthesia, should be done. We use *local* in the form of abdominal "block" and find it highly satisfactory. We do not use spinal in these patients. In cases where collapse therapy has been practiced, particularly thoracoplasty, we believe cesarean section, using *local* block anesthesia, should be more frequently employed. Certainly in the primipara this procedure would obviate the relatively long first stage and prevent the respiratory embarrassment that comes with strong second stage pains in the patient who has only one, or perhaps less than one useful lung. Furthermore, cesarean section is the method of choice when cardiac or nephritic lesions, excluding, of course, eclampsia, complicate the pulmonary status. It goes without saying that if cesarean section is to be the method of choice it should be performed by a competent operator in a well equipped operating room. Vaginal cesarean section should *never* be done after the seventh month of gestation, because even in expert hands, the trauma and blood loss associated with this operation are considerable. This not infrequently causes an extreme degree of

shock which in turn is distinctly injurious to the tuberculous patient, especially in the advanced exudative and pneumonic forms of the disease.

These patients must be protected against long, tedious, exhausting labors and difficult, traumatic, or operative deliveries, performed late in labor when the more conservative plan of delivery has failed. Here, as elsewhere in clinical medicine, conservatism may turn out to be radicalism when not tempered with good judgment. To make labor as comfortable and non-exhausting, and delivery as easy, short and nontraumatic as possible, is a good working rule. These facts cannot be too strongly emphasized and I dwell upon them because I believe the accoucheur—general practitioner and specialist—has had to take the blame far too frequently for the reactivation of a healed tuberculous lesion or the spread of an active one that the phthisiologist had under control. Furthermore, it must be constantly kept in mind by the accoucheur that hemorrhage and shock should be prevented as far as it is possible to do so and that when they occur, prompt and vigorous treatment is urgently indicated. Transfusion should be given without delay, or without regard for the tuberculosis, and in sufficient quantity to replace the blood loss. Shock cannot be successfully combated until the blood vessels have their fluid loss (plasma) restored. Prevention of hemorrhage and shock or shock without hemorrhage is the working axiom in this connection. Remember, in every obstetric procedure, Dr. De Lee's oft repeated slogan "conserve blood."

#### MANAGEMENT OF THE PUERPERIUM

The obstetric management of the tuberculous patient during the puerperium is essentially the same as for any other patient. The phthisiologist accepts full responsibility for the tuberculosis. In the milder healed lesions nothing need be done except repeated check-up of the tuberculosis and "watchful waiting" to be sure reactivation has not taken place. In cases

where collapse therapy has been practiced prior to and during pregnancy it should be carried out during the puerperium for as long as indicated. There may be cases where collapse therapy is indicated for the first time immediately after delivery. In other cases only some form of abdominal compression as obtained with the diaphragm lift which elevates and restricts the movements of the diaphragm may be necessary. We have used the Burgess Gordon type of abdominal compression binder with satisfactory results. It can be used in all cases—non-collapsed and collapsed—immediately following delivery and for as long as indicated.

Excessive postpartum bleeding is not uncommon in the tuberculous parturient. Matthews and Bryant in 317 ex-Trudeau patients reported a 13 per cent incidence of postpartum hemorrhage, whereas the incidence for the general population is 2 per cent. These data, however, were obtained from the patients, not the doctors who delivered them, and may be subject to inaccuracies. Nevertheless, other writers have reported a definitely increased incidence in postpartum hemorrhage of greater or less severity, particularly in advanced tuberculosis where the patient is in poor general condition. Consequently this accident must always be kept in mind. Prompt and appropriate treatment for the control of excess bleeding, including blood transfusion is the proper procedure. Furthermore, the accompanying shock must be promptly combated by morphine, application of heat to the entire body, hypertonic intravenous dextrose (300 c.c. of 25 per cent solution) followed by blood transfusion. Delay in these procedures may well mean the difference between life and death in the mother who has advanced tuberculosis. With the modern methods of handling the tuberculosis, the pregnancy, the labor and the delivery, the puerperium *per se* does not present the hazards that it formerly did, provided, of course, these methods are available. Furthermore, it is more generally recognized today that

proper care must be given the tuberculous mother following the postpartum period for a sufficient length of time to make it safe for her to return home. The puerperium is often a critical period for the non-tuberculous parturient and in the presence of tuberculosis the most careful supervision is definitely indicated.

#### LACTATION

Of the many questions relating to the effects of pregnancy and parturition on tuberculosis, nursing is one phase that should demand most careful consideration. The baby should never be allowed to nurse, except perhaps in those cases where the mother has a minimal or moderately advanced healed lesion with a negative sputum. If she is in good general condition and it is highly desirable to give the baby a good start in life, lactation may be permissible. In such cases the baby may be nursed from six to eight weeks *only*. All others should *absolutely not* be nursed. The objections to nursing are, of course, the danger of infecting the child and the added drain upon the mother's strength. The possible ill effects on the recently delivered tuberculous mother of the extra work and worry of the household, particularly under strained economic conditions, are perfectly evident to the practical clinician. A "break-down" in the mother may just as well be due to child-rearing as to child-bearing. Nowadays, fortunately for these mothers, weaning the baby is not the serious problem that it was in former years. The pediatricians are more expert in feeding babies artificially, and are no longer skeptical regarding their survival, future development and longevity. Many reports substantiate this point of view. For example, Matthews and Bryant showed that out of 579 children 556 were alive fifteen years or more after birth, and 501 (86.5 per cent) of these were in good health; fifty-five (9.5 per cent) were below par in health and in only nine cases of tuberculosis were found or suspected. Barnes and Barnes state that 81 per cent of children born of

tuberculous mothers are healthy and develop normally. Blisnjanskaja found that of 23,000 children taken from their tuberculous mothers and sent to the country, only seven developed tuberculosis (Jameson).

#### WHEN SHALL THE TUBERCULOUS PATIENT CONTEMPLATE PREGNANCY?

Another very important question that inevitably presents itself for consideration is: How long after "arrest" of the tuberculosis should a patient wait before assuming the responsibilities of pregnancy, labor and the puerperium? This will vary, of course, because of the multiplicity of factors concerned. However, it can be said that with the average run of tuberculous patients, from two to five years should elapse before pregnancy is contemplated. Generally speaking, in minimal or moderately advanced cases with the productive or fibrous type of lesion, from one to two or more years should be allowed, whereas with the exudative or pneumonic types three to four or more years may be necessary. Naturally, in the far advanced cases still more time, four to five or more years will be required. There will be patients who should never become pregnant because of the undue risk involved, while, on the other hand, there will be patients who will have several children. In fact we have seen several such women who have experienced no appreciable harm to their tuberculosis. This question, in its final analysis, must be decided by the coöperating phthisiologist and accoucheur after a thorough consideration of the pathologic lesion in each individual case, not overlooking the temperament, desires, wishes and willingness to coöperate of the patient herself. In other words, individualization of each case based on its own merits, as elsewhere in medicine, is the best and safest criterion upon which to base prognosis.

#### STERILIZATION

The question of sterilization of the tuberculous woman—nullipara or multipara—is important, first from the view-

point of the mental effect on the patient herself and secondly from the standpoint of the tuberculosis. There is always present the likelihood of complete "arrest" of the tuberculosis, in which case we are fairly sure that after an interval of two or three or four or more years pregnancy and parturition can take place without undue risk. For the woman who already has her family, however, the indication is clear; we have only to decide upon the method.

It is, of course, common knowledge that when women menstruate, no matter what else may plague them, they seem more content with their lot in life. Therefore, we believe castration by means of the x-ray or radium irradiation is contraindicated except in those in whom menstruation is slowing up to an unreasonable degree the recovery from their tuberculosis. In a number of young women in whom the slowing up process has been pronounced, I have advised temporary castration (a few months to two years or longer) with x-ray or radium irradiation and with very satisfactory results. One such patient later became pregnant, carried to term, and was delivered of a normal child without any apparent effects on the tuberculosis. Where simple tubal ligation is performed to prevent conception there is not the same disturbing element, since menstruation is not interfered with.

Contraceptives, of course, are employed and with good success, depending on the physician's advice, his knowledge of technique and the ability of the patient to cooperate. However, fear of pregnancy and the difficulty of getting multiple abortions performed, makes this form of birth control unpopular with a great many tuberculous patients. Those who have far advanced tuberculous lesions and do not wish to become pregnant or have been advised not to become pregnant had best be sterilized by whatever method seems most suitable.

#### SUMMARY

Every woman cherishes the hope of motherhood. The desire to reproduce is

instinctive. She should therefore not be deprived of this hope unless there is no alternative. Sweeping statements cannot, with sincerity and honesty, be made regarding pregnancy in tuberculous women. We have no right to say "no woman with tuberculosis should bear children" nor can we say "pregnancy, labor and the puerperium have no influence on the course of tuberculosis." There is, however, "a middle of the road" attitude that can be assumed and with a reasonably thorough understanding of both the associated conditions we may look forward to the successful outcome in a large proportion of cases. Success, however, will very largely depend upon the status (active or inactive), the type or character and extent of the tuberculous lesion; the *economic status* and the *attitude* of the patient; the thoroughness with which the phthysiologist can control the lesion; the completeness of prenatal care and the adequacy with which the obstetrician manages the delivery and the puerperium. Without the complete coöperation of all concerned, particularly the phthysiologist who understands the pregnancy but disregards it and the obstetrician who is interested in tuberculosis, but sticks to obstetrics, the prognosis will remain uncertain. On the other hand, with full coöperation, along with the modern methods of case finding, diagnosis and treatment of tuberculosis and the improvement in obstetric care that is now generally recognized, the problem of the relation of tuberculosis to obstetrics will not be so troublesome and uncertain as in the past.

This relationship will not show satisfactory results, however, until better provision is made in every community for the proper care of the pregnant woman who has tuberculosis. Under the present set-up, case finding efforts, expert diagnosis and adequate management can only be carried out in the favored communities that possess the proper facilities and personnel. Surely it is not humane to continue to care for the pregnant tuberculous patient in the desultory and inadequate manner that

many of us have had to employ in the past. We need a keener appreciation of the facts by the general public; by those in control of hospitals and sanatoria; and, most of all, by the medical profession.

## REFERENCES

1. NICHOLSON, E. E. National Tuberculosis Association Social Series No. 7. Revised Ed. 1938.
2. National Tuberculosis Association. Diagnostic Standards, 1938.
3. DICKINSON, R. L. Personal communication.
4. HENSKE, A. C. *J. Missouri M. A.*, 35: 430, 1938.
5. ADAIR, F. L., and STIEGLITZ, E. *Obstetric Medicine*. Philadelphia, 1934. Lea and Febiger.
6. ORNSTEIN, G. G., ULMAN, D., and DITTLER, E. *Am. Rev. Tuberc.*, 23: 248, 1931.
7. HILL, ALICE M. *Am. Rev. Tuberc.*, 16: 157, 1927.
8. WHITNEY, J. S. Personal communication.
9. PREST, C. S. Personal communication.
10. ORNSTEIN, G. G., and EPSTEIN, I. G. *Quart. Bull. Sea View Hosp.*, 4: 420, 1939.
11. JAMESON, E. M. *Gynecological and Obstetrical Tuberculosis*. Philadelphia, 1935. Lea and Febiger.
12. BOQUIST, H. S., SIMONS, J. H., and MYERS, J. A. *Am. Rev. Tuberc.*, 31: 48, 1935.
13. ORNSTEIN, G. G., and KOVNAT, M. *Am. Rev. Tuberc.*, 31: 224, 1935.
14. MATTHEWS, H. B., and BRYANT, L. S. *J. A. M. A.*, 95: 1707, 1930.
15. MATTHEWS, H. B. *Am. J. Surg.*, 35: 293, 1937.
16. BARNES, H. L., and BARNES, L. R. *Am. J. Obst. & Gynec.*, 19: 490, 1930.
17. STANDER, H. J. *Williams' Obstetrics*, 7th ed. New York, 1936. Appleton.
18. VON FRISCH, A. *J. Egyptian M. A.*, 22: 170, 1939.
19. JAMESON, E. M. *Am. J. Obst. & Gynec.*, 36: 59, 1938.
20. MARSHALL, G., et al. *Brit. M. J.*, 1: 140, 1931.
21. GORDON, BURGESS. *Am. Rev. Tuberc.*, 32: No. 6, 1935.
22. AMBERSON, J. B., and STUDDIFORD, W. E. *Preventive Medicine. N. Y. Acad. Med.*, Jan. 1938.
23. SEELEY, W. F., SIDDALL, R. S., and BALZER, W. J. *Am. J. Obst. & Gynec.*, 37: 741, 1939.
24. SEELEY, W. F., et al. *Am. J. Obst. & Gynec.*, 39: 51, 1940.
25. MYERSON, M. C. *Quart. Bull. Sea View Hosp.*, 4: 339, 1939.





# CARDIAC DISEASE IN OBSTETRICS

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DISEASE in a pregnant woman is not the same in its course and results as in the non-pregnant patient. Though the name of the disorder may be the same, the coincidence introduces new and variable factors which drastically alter the manifestations and the diagnostic, prognostic and therapeutic problems. Gestation brings about physiologic changes in the prospective mother which may, and often do, change her vulnerability to certain diseases and also modify the homeostatic reactions and compensatory phenomena. Certain pathologic conditions may arise which are peculiar to, and definitely associated with, the pregnant state. Furthermore, in obstetric medicine the problems of the attending physician are made more complex by the fact that two lives are involved. A dual viewpoint is essential if the full significance of these important and frequent problems is to be grasped. The obstetrician views the cases as those of pregnancy complicated by some coincident disease, whereas the internist inevitably reasons that these are cases of disease complicated by pregnancy. Either viewpoint alone is inadequate, for both are correct, yet individually incomplete. On the one hand the question arises as to what effect does or will pregnancy have upon the course of the disease, and on the other its corollary exists: what effect will the disease have upon the gestation and/or the products thereof? The answers to these pertinent questions and the application of such knowledge will vary with each and every one of the innumerable possible complicating coincidences. For example, it is well known that an active syphilis in a pregnant woman will cause serious or even fatal damage to the fetus, though the course of the maternal syphilis shows little change. In contrast, an active ma-

ternal tuberculosis rarely affects the fetus, but the pregnant state may lead to disastrous activation and exacerbation of the maternal infection. Thus the vexing question often arises as to the advisability of prematurely terminating pregnancy in order to safeguard the life or health of the mother. These decisions, as those involving the prevention of pregnancy, include social, legal, ethical or religious and psychologic questions as well as the more purely biologic or medical ones.

Many of the problems of obstetric medicine<sup>1</sup> arise prior to conception and the pregnant state; others arise during gestation, either coincidentally or with some etiologic association between pregnancy and the disease in question. In the former group of disorders it is often possible to foretell of later difficulties; frequently disaster is predictable if there is sufficient clinical acumen and judgment to evaluate correctly the significance of certain preconceptional disturbances. Disease arising during pregnancy is predictable less frequently, but it must never be forgotten that pregnancy per se confers no immunity upon the prospective mother; her vulnerability to disease is more often increased than decreased or unaltered.

Premarital or preconceptional health evaluation has become increasingly frequent and definitely more thorough, a definite advantage, for certainly there are few places in clinical medicine where forewarning is more valuable than in the practice of obstetrics. Public consciousness is awakening to the importance of such prophylactic health examinations, but the understanding is incomplete and unnecessarily limited. The obligation to foster and enhance the public's appreciation of thorough periodic health evaluation falls upon every practitioner of medicine. Certain

examinations are expected by the better informed patients; other equally important aspects are completely ignored because of perfectly natural ignorance. Such ignorance, however, is inexcusable in the physician. Serologic examination for syphilis is becoming a routine procedure before marriage; in many states it has been made obligatory by law. Search for evidences of heart disease is anticipated by the majority of young women requesting a preconceptional or premarital examination. On the other hand, many physicians and almost all patients are satisfied with a very superficial examination of the urine as evidence of adequate renal function. Such evidence is wholly inadequate<sup>1,2</sup> and, consequently, severe and dangerous renal disease is more frequently an unexpected problem in obstetric practice than cardiac disease. Both the heart and the kidneys are subjected to greatly increased physiologic burdens by pregnancy and it is only logical that the functional capacity of both structures should be carefully evaluated *before* these strains are imposed.<sup>3</sup>

Health inventory requires clinical skill, judgment and thorough, painstaking diagnostic study. In the acutely ill patient symptoms and signs are usually obvious and diagnosis is largely a question of elimination of the less probable explanations for the clinical picture, and proof that the chosen reason (diagnosis) is the correct one. Effective evaluation of the health and functional reserve capacity of an apparently well individual requires the discovery of obscure hints and occult evidences of early impairments, and the detection of suggestions of potential disease. Perfect physical fitness is exceptional. Although the great majority of abnormalities discovered by health evaluation studies are inconsequential, in preconceptional clinical examination they must be appraised with due consideration of the particular physiologic stresses imposed by the anticipated pregnancy. With such considerations in mind it is obvious that many findings may assume significance which ordinarily would

be wholly immaterial. To do this well does not require any very special training, but it does involve conscientious thoroughness, time, and an understanding of the physiologic changes occurring in pregnancy.<sup>1</sup>

Unfortunately, many physicians consider health examination and physical examination as synonymous. The physical examination is but a part of the clinical study which constitutes a proper health evaluation. Of almost equal importance is the elicitation of the history of the patient and the intelligent appraisal of the data revealed. The history of past illness frequently reveals disease potentialities. For example, pyelitis in the past may be a forewarning of impending recurrence; a history of severe migraine with frequent bouts of debilitating nausea and vomiting may herald excessive vomiting in the first trimester of pregnancy. Likewise, evidence of rheumatoid phenomena in childhood should incite an especially careful search for evidences of rheumatic carditis and/or latent chorea. Such information is rarely volunteered by the patient; it must be extracted by prolonged and meticulously specific inquiry. The value of the history of the apparently well patient who is requesting a preconceptional prognostic opinion is not limited to the data regarding previous sickness: the psychologic and socio-economic background and the habits of the individual are of great importance, particularly when some organic defect may require prolonged limitation of activities or special care. In perplexing cases, where one is in doubt as to the advisability of the patient's attempting pregnancy but hesitates to deny a woman her priceless privilege of motherhood, the socio-economic status may be the deciding factor. Whereas one patient has the means, the patience and the character to follow rigid and prolonged restrictions of physical activities, another may be temperamentally or economically unable to take proper care of herself either during or after her pregnancy. It must not be forgotten that frequently a baby

requires far more physical effort from its mother after it is born than before.

In addition to the physical examination and the patient's history, laboratory studies are a third source of invaluable information. The appropriate extent and character of these examinations will depend largely upon the information elicited by the other two methods of fact finding, although a certain minimal routine is advisable. A serologic test for syphilis, urinalysis and complete cytologic study of the blood constitute the barest minimum. Should the history indicate the probability of previous renal injury, as from scarlet fever or diphtheria in childhood, tests planned to evaluate the kidney functional capacity are indicated.<sup>2</sup> Discovery of anemia, even of low grade, warrants further investigation into its probable cause. These are suggestive illustrations of the comprehensiveness of an adequate health evaluation made prior to pregnancy. The discovery of heart disease likewise makes further study imperative.

The older and traditional pessimistic outlook for all women with heart disease contemplating marriage and motherhood is unwarranted. Yet it is safer to err on the side of conservatism and lay all the facts upon the table; the patient, after all, is the one who must make the final decision. As physicians attempting prophylaxis we can only advise. There are many women who apparently prefer to "diaper their way into heaven" despite emphatic forewarning of the excessive risks of repeated pregnancies. The gift of motherhood must never be denied without good and sufficient reasons. The patient is entitled to know of these reasons so far as her education and intelligence permit her to understand them.

Even more frequent is the problem of deciding the advisability of additional pregnancies in women who have already been pregnant one or more times. If the previous gestations failed in fulfillment because of death of the fetus or the loss of a child, the yearning for motherhood may be greatly intensified. On the other hand, if

there are already one or more children at home we must consider these responsibilities in advising concerning the safety of further childbearing. For a childless woman knowingly to "take a chance" involves only her and her husband. For a mother of a family knowingly to subject herself to grave risks (having been conscientiously forewarned) involves far greater responsibility. A great many other factors are also involved, such as the patient's age, the history of difficulties with previous pregnancies and the frequency of her pregnancies. An interval of *at least* two years, and preferably three, should elapse between pregnancies in any woman with previously compensated organic heart disease, no matter how well compensated the heart may be. There is no substitute for time in the processes of readjustment and repair after strain.

When reasons exist to make pregnancy truly hazardous it does not suffice merely to declare: "No (more) babies for you!" The patient is entitled to learn both why and how this is to be accomplished; the physician shirks his responsibilities if he does not give advice regarding contraceptive protection after such a decision.

#### INCIDENCE AND MORTALITY OF CARDIAC DISEASE IN OBSTETRICS

The incidence of all types of heart disease in obstetric patients is approximately the same as for the same age group in the population as a whole. Statistical reports place this incidence at from 1.5 to 2 per cent. The frequency of rheumatic carditis in young women is definitely greater than among men of similar age. The ratio is about 4:3. Apparently young girls with rheumatic heart disease have a somewhat better chance to reach the age of maturity (and child-bearing) than do boys similarly afflicted.

The great majority of organic lesions of the heart observed in obstetric practice are of rheumatic etiology. Congenital heart lesions, hypertensive disease of the heart, luetic carditis, pericarditis and the rare

instances of coronary arteriosclerosis in the more elderly patients all together represent less than 10 per cent of the total. Functional disorders, including paroxysmal tachycardia, the several arrhythmias and thyrotoxic disturbances, are common, but rarely so urgent as organic disease. It is notable that approximately half of the maternity patients with organic heart disease have no knowledge of the cardiac disorder prior to its discovery on prenatal examination. This emphasizes the urgency of popularizing preconceptional examinations.

The direct mortality from heart disease in pregnancy varies greatly in the many reported studies. Among the factors which contribute to the variation in these data are differing diagnostic criteria, incomplete records, and, especially, dissimilar classifications as to the cause of death. One comprehensive statistical survey<sup>4</sup> states that the average immediate death rate among obstetric cardiac patients is 4.3 per cent. Other reports<sup>5</sup> place the mortality between 5 and 10 per cent. These figures are misleadingly low, for the deaths from pneumonia, embolism, sepsis and nephritis in obstetric patients are very greatly increased when pregnancy is complicated by heart disease. Congestive failure accounts for at least 70 per cent of the direct fatalities from cardiac disease in obstetric practice. It is notable that about 75 per cent of the fatal cases survive delivery. In half of these the termination of pregnancy is premature. The greatest number of deaths occur within twenty-four hours after delivery.<sup>4</sup>

The outlook for primiparous and multiparous women with heart disease is not the same. With each successive pregnancy the chronic cardiac patient becomes a poorer and poorer risk. The stress of repeated pregnancies accelerates depreciation of the cardiac reserve. Much of the damage done by pregnancy to a heart previously injured is permanent and irrevocable. This is not revealed at all by the data concerning the immediate mortality. We may conscien-

tiously state, although numerical proof is lacking, that the delayed mortality and morbidity are more significant hazards than the immediate risks. Even with limited follow-up studies, it has been observed<sup>5</sup> that nearly half the patients were definitely worse after pregnancy. It is impossible to estimate accurately just how much the lives of many cardiac patients are shortened by pregnancy and labor, but the total must be considerable. These delayed consequences are rarely seen by the obstetrician; the internist and general practitioner are called upon to attempt the miracle of rehabilitating an irrevocably damaged heart months or a very few years after pregnancy and labor have hastened the onset of failure.

#### PHYSIOLOGIC CONSIDERATIONS

In normal pregnancy the work of the heart is definitely increased. Under certain abnormal conditions this increment in the cardiac burden is considerably augmented. Undue obesity, arterial hypertension, respiratory disorders, anemia and excessive uterine enlargement (twins or polyhydramnios) are some of the frequent complicating phenomena which add tremendously to the cardiac load. In evaluating the probable increase in work for the heart in pregnancy the likelihood of such complications must not be ignored.

In a perfectly "normal" pregnancy the increment of cardiac labor is considerable, especially during the latter months of gestation, and most particularly during labor. Many factors contribute to this. The minute volume of blood flow from the heart is increased on the average 27 per cent in the last half of pregnancy; in some instances this increase amounts to as much as 50 per cent.<sup>6,7</sup> The blood volume is likewise increased; it becomes from 20 to 25 per cent greater at term than prior to pregnancy.<sup>8</sup> This is due to an increase in both the cell and plasma volumes. There occurs also a very considerable increase in the venous pressure,<sup>7</sup> especially in the pelvic and

femoral veins. The oxygen consumption is increased, both because of the high anabolic activity of the rapidly growing fetal tissue and because the maternal metabolic rate is likewise elevated as pregnancy advances.

The increase in weight which is inevitable in normal pregnancy adds to the cardiac load, particularly upon physical effort. Respiratory exchange is diminished by the handicap of relative diaphragmatic immobility in the later weeks of gestation and by the forced high position of the diaphragm. The vital capacity is diminished, especially just before the relief of the excessive abdominal distention which comes with lightening. Frequently dyspnea on exertion is distressing despite essentially normal cardiac function. Obviously a concomitant anemia, even of slight degree, will greatly augment these additional burdens placed upon the circulatory apparatus.

It is surprising, with the demands placed upon the heart by the purely physiologic changes of pregnancy, that true cardiac hypertrophy does not occur. Repeated clinical and experimental studies indicate that no true hypertrophy does occur. The superficial clinical impression is likely to be that enlargement has taken place in the last trimester of pregnancy, but this is due to the changes in cardiac position engendered by the pressure of the high diaphragm. This displaces the heart to the left; the apex impulse may be as much as an inch beyond the midclavicular line. Although the transverse position of the heart increases the area of cardiac dullness elicited on percussion, there is not a true hypertrophy.

Where pre-existing heart diseases occur, the increased cardiac burdens of pregnancy are prone to induce more serious consequences. Hypertrophy existing before the introduction of these additional loads is accelerated and dilatation and congestive failure are all too frequently induced. Pre-existent heart disease is exacerbated by pregnancy. Intoxication, hypertension, anemia, anoxemia and histanoxia are not infrequent additional insults.

#### DIAGNOSIS OF CARDIAC DISEASE IN PREGNANCY

Diagnosis consists of far more than merely giving a name to a disorder. This is particularly true of heart disease. A comprehensive diagnosis to be fully useful must include consideration of the *pathology* of the lesion or lesions, the *etiology* and the degree and type of *functional impairment*. Diagnosis therefore has quantitative as well as qualitative attributes. One must also consider whether or not the etiologic factors are inactive or still active, and, if inactive, whether they are likely to be reactivated. Such impression is essential to the proper and intelligent treatment of cardiac problems in obstetric patients.

Examination of the heart may reveal physical findings deviating from the normal without there being any actual disease of the heart. Anemia will cause so-called "hemic murmurs," the raised diaphragm will distort the area of cardiac dullness, and nervous disorders may induce arrhythmias in the absence of organic heart disease. It must never be forgotten that the diagnosis of "heart disease" carries with it to the patient a connotation which may cause severe emotional or mental damage. It therefore behooves the physician to be cautious and positive, especially in pregnant patients, who are particularly vulnerable to psychic upsets. The lay public visualizes "heart disease" as a dread malady which strikes its victims down with dramatic and tragic suddenness. The physician more frequently sees in the term the nearly inevitable, though often long delayed, picture of congestive failure with edema and orthopnea.

The criteria necessary for diagnosis of heart disease have been very carefully and extensively reviewed by the Criteria Committee of the New York Heart Association.<sup>9</sup> Extended review of their conclusions is not necessary here, but it should be emphasized that the presence of some one or more of the following pathognomonic evidences is requisite for the diagnosis of organic heart disease:

1. Serious arrhythmia, such as auricular fibrillation, flutter, heart block or alternation of the pulse.

2. Diastolic thrills and/or murmurs, together with other evidence of valvular (mitral or aortic) deformity.

3. Increased area of aortic or cardiac dullness with displacement of the apex impulse.

4. Hypertensive disease, thyrotoxicosis, chronic nephritis or signs of arteriosclerosis, with or without hepatic enlargement.

5. The classical syndrome of angina pectoris.

The *anatomic diagnosis* will depend largely upon the physical signs elicited. In pregnant women, especially during the later months of gestation, there are a number of factors which distort the normal physical findings, as already discussed. Special care must be exercised in evaluating the observations. The enlargement of the breasts frequently makes both auscultation and percussion relatively unsatisfactory. Nevertheless, any physician competent to diagnose organic heart lesions in non-pregnant patients is competent to do so in obstetric cases.

*Etiologic diagnosis* depends largely upon the data derived from the patient's history, although associated physical and laboratory observations are also of great value. Hypertensive heart disease is not observed in the absence of long standing hypertension.<sup>3</sup> Serologic evidence of syphilis is confirmatory when cardiovascular lues is suspected. Determination of the basal metabolic rate may be necessary to determine the etiologic relationship of suspected thyrotoxicosis. But, in obstetric patients, 90 per cent of the cases of heart disease are of rheumatic origin. Careful inquiry is essential to elicit information regarding the frequency, severity, duration and recency of acute rheumatoid manifestations, such as tonsillitis, rheumatic arthritis or chorea. These data indicate the latency or activity of the original infection and thus forewarn as to the likelihood of acute recurrences during the pregnancy.

The last part of the diagnosis, the evaluation of the degree of *functional impairment*, is the most important of all. It is upon these conclusions that both prognostic and therapeutic decisions will be based. The recently revised American Heart Association Classification of cardiac functional capacity<sup>9</sup> is indubitably the most useful and pragmatic system of indicating the functional reserve. Patients fall into the following classes of diminishing functional reserve:

*Class I.* No limitation of physical activity. Ordinary effort induces no distress. Physical findings are the only evidence of heart disease.

*Class II* (Formerly Class *IIa*). Cardiac disease patients with slight or moderate limitation of physical activity. Ordinary effort induces discomfort.

*Class III* (Formerly Class *IIb*). Patients with cardiac disease with greater limitation of physical activity. Less than ordinary effort induces distress.

*Class IV* (Formerly *III*). Patients with heart disease unable to carry on any physical activity without discomfort. Decompensated patients.

Before the World War clinical conclusions about heart disease were derived almost solely from the diagnosis of the anatomic defects. MacKenzie<sup>10</sup> was the first to point out the fallacy of such reasoning and emphasize the importance of the functional capacity of the heart as an index of its ability to carry through pregnancy successfully. The above classification, developed largely through the efforts of Pardee, is a refinement of the original conceptions of MacKenzie.

Cardiac patients falling into Class *I* are good obstetric risks, barring the coincidental presence of other complications. These patients respond to effort without undue dyspnea or distress. The simplest way of measuring circulatory efficiency and cardiac reserve is to determine the amount of effort necessary to induce dyspnea. It is immaterial just what procedure the physician adopts to determine this,<sup>11</sup> so long as a

routine test is used and he knows the range of response in normal individuals. It is not the severity of the dyspnea which is significant, but the effort required to induce it. This information is frequently most easily and accurately derived from the patient's *history*, for in her daily routine the psychic factors of "a test" are absent and the variations of the reserve from day to day are averaged.

Patients in Class II may go through pregnancy without too grave risks, if they obtain the requisite rest and avoid those exertions which induce distress. They require, however, frequent and conscientious prenatal care. Those women who fall into Class III are poorer risks; frequently they require weeks of continued bed rest in the latter part of pregnancy and must be prepared for the efforts of labor by judicious medical treatment. The maxim "To catch heart failure early, examine patients often" must ever be before one. As the load of pregnancy increases the diminution of avoidable burdens may not suffice to keep the strain within the limits of the cardiac reserve. In such patients cardiac failure may supervene despite constant bed rest.

Decompensated pregnant patients (Class IV) are critically and dangerously ill. Their reserve for exertion is nil. Any additional burden upon the heart, such as surgical interference or labor, may precipitate sudden exitus.

Recalling that as pregnancy advances the labor of the heart increases and that functional reserve is best measured by the response to increased effort, one can readily understand the logic of the clinical rule that *the earlier in pregnancy the signs of circulatory embarrassment arise the smaller is the functional reserve and the more precarious the prognosis*. This axiom is equally valid in considering the margins of safety when preëxisting diseases have reduced the functional reserve of other structures than the heart.<sup>12</sup> Frequent and conscientious prenatal observations are the keystones

upon which safety for the pregnant cardiac patient must be maintained.

Certain complications may rapidly and extensively affect the prognosis and require modification of therapy which might be otherwise based on functional impressions alone. Auricular fibrillation, embolic phenomena, activation of infection by bacterial endocarditis,<sup>13</sup> intercurrent systemic infection, the development of arterial hypertension and/or renal disease and the appearance of shock with or without hemorrhage are among the not infrequent complications which may suddenly throw all previous prognostication and therapeutic programs into chaos.

#### TREATMENT OF CARDIAC DISEASE IN PREGNANCY

All therapy must follow three fundamental principles. These are: (1) therapy directed against the etiologic factors: etiologic therapy; (2) therapy to reduce the physiologic burden of the injured structures to permit of physiologic compensation and repair: rest; and (3) therapy to maintain or improve the tissue nutrition and respiration. In the clinical application of these principles of therapeutics the relative importance and urgency of the three may vary considerably. For example, in thyrotoxic heart disease the etiologic attack through correction of the hyperthyroidism is of the greatest significance. On the other hand, instances of congenital cardiac defects or valvular deformities from long inactive rheumatic endocarditis are not amenable to effective etiologic therapy. Similarly, in congestive heart failure, therapy directed against the remote etiology is of little avail, but rest and the improvement of tissue nutrition and respiration by insuring an adequate glucose<sup>14,15</sup> and oxygen supply are often life saving. For therapy to be fully effective it is essential that none of these three principles be forgotten or ignored. Curative therapeutics depend largely upon correction of etiology. This presupposes accurate etiologic diagnosis. It is illogical to antici-

pate rehabilitation and repair of injured structures unless they are assured of adequate supplies of nutriment and oxygen.

The treatment of Grade I (fully compensated) heart disease in pregnancy is largely prophylactic. The cardiac lesion alone does not justify interference, and natural delivery is the rule. Though these patients may complain of some dyspnea and pedal edema in the last trimester of pregnancy, these phenomena need cause no alarm; they occur in patients with normal hearts. However, even fully compensated cases of valvular disease should be observed carefully and often. Any abrupt acceleration of the basal pulse rate, elevation of the arterial tension, exacerbation of edema or coughing is an indication for immediate restriction of activity.

The opportunity for etiologic therapy is limited. It is important to search for foci of infection, such as alveolar abscesses, which may be adding further insult to the previously damaged myocardium. Dental therapy and extraction during pregnancy are safe. They constitute a lesser evil than the neglect of foci of infection.<sup>1</sup> Though it may not be necessary to curtail the normal activity of these patients, they should be cautioned to avoid unnecessary or violent exertion. The cardiac efficiency certainly is not improved by pregnancy and as the cardiac load increases continuously, the reserve margin is constantly narrowed.

Application of the third principle of therapeutics is often of the greatest prophylactic value. A moderate anemia is a frequent concomitant of pregnancy<sup>16</sup> and any diminution of the hemoglobin content of the blood greatly increases the effects of circulatory handicap. Compensated mitral valvular disease is usually associated with a moderate increase in the hemoglobin over the normal; any fall thereof may be decidedly embarrassing to the heart. Therefore, frequent prenatal check-ups of the hemoglobin and blood counts are highly desirable. Prompt anti-anemia therapy with diet, iron and active liver preparations<sup>17</sup> is indicated whenever depletion

begins to appear. It does not pay to wait for severe anemia to add serious complications.

The diet must be adequate, not only as regards protein, carbohydrates, fats and minerals, but also with sufficient vitamin content for both the mother and the rapidly growing fetus. It has been shown<sup>18</sup> that vitamin B<sub>1</sub> deficiency is a causative factor in certain cardiopathies arising in pregnancy and that liberal administration has prophylactic value. Protein restriction is prone to aggravate anemia.

The management of patients with Grade II functional capacity (fairly compensated) involves some new problems. Activity may have to be more restricted to keep the cardiac load at a minimum. More frequent prenatal inventories are desirable. Meticulous attention to secondary potential sources of further cardiac insult is important. Prolonged convalescent bed rest after any mild transient intercurrent infection, such as coryza, grippe and the like, is vitally important if additional damage to the myocardium is to be avoided. The patient must be taught to watch closely for the appearance of warning signals such as undue dyspnea, precordial distress and increasing pedal edema. She *must* stop when these appear. Sometimes periods of complete rest in bed for weeks are necessary to restore circulatory compensation. In Class III (poorly compensated cases with a small margin of safety), hospitalization, absolute rest and nursing care are requisite. Patients in this class must be under constant observation during the postpartum period. All cardiac patients are best kept in bed at least ten (and better more) days before the date of expectancy.

The choice of obstetric procedure in these gravid cardiac cases is often difficult; many factors enter into the decision as to whether pregnancy is best terminated by normal delivery, premature induction of labor, cesarean section or abortion. Of critical importance is the prognostic impression concerning whether the patient is exposed to a greater danger and increased irreparable and irrevocable cardiac damage



if gestation is permitted to continue. Prognostication as to the reserve for the strain of labor is best made at the last possible moment. Labor is often precarious for the cardiac patient; the choice is that of the probable lesser evil. No labor is easy, despite the oft repeated platitude that "cardiac disease patients have easy labors." Labor introduces strains of unpredictable intensity and duration. Of the many factors which must be considered in connection with the choice of method of delivery, the degree of compensation, the arterial tension, the condition of the blood, the pulmonary findings, the obstetric condition of the pelvic passages, the parity of the patient and the skill of the obstetrician are of major importance. Each problem must be considered individually; generalizations and routine management are impossible.

The earlier in pregnancy signs of failing compensation appear, the narrower is the margin of safety. If evidence of failure appears before the sixteenth week, termination of pregnancy by therapeutic abortion is unquestionably the wisest course.<sup>19</sup> The likelihood of survival of either the mother or the fetus in such instances is almost nil; early abortion offers the woman better chance of survival. The borderline cases or patients who refuse such life-protecting measures can occasionally be carried on to the point of fetal viability and delivered well before full term by cesarean section, followed by sterilization. The risks of such a program, however, are very great.<sup>20</sup>

It cannot be overemphasized that *operative procedures should never be undertaken upon decompensated patients (Class IV) without a proper course of medical treatment.* The cardiac condition is more urgent and critical than the obstetric problem. The induction of abortion is never justified during cardiac decompensation.

If labor should begin naturally (either at term or prematurely) in the presence of congestive failure, morphine should be administered in the hope of delaying delivery by the arrest of uterine contractions until the circulatory conditions have

been made more favorable by intensive medical therapy.<sup>21</sup> The dread complication of congestive failure arising during labor is often heralded by a sudden fall in the arterial tension and a rise in the pulse and respiratory rates. Such signs are grave indications of impending disaster; the obstetrician must devote his energies to procedures which will ease the strain upon the exhausted heart while the internist combats the circulatory emergency. Pulmonary edema, as evidenced by moist râles in the lung bases, is best attacked by subcutaneous injections of small repeated doses of atropine sulfate (gr.  $\frac{1}{150}$  to gr.  $\frac{1}{50}$ —0.4 mg. to 1.3 mg.). Digitalis should be administered intravenously until full digitalization is attained. Late nausea and vomiting from over-digitalization are better than a fatality due to inadequate dosage.<sup>21</sup> Blood loss should be kept at a minimum. The withdrawal of blood by phlebotomy to relieve congestive failure in an undelivered woman in labor or near term is a practice fraught with danger. The amount of blood which may be lost during labor or immediately thereafter is never predictable. Frequently the edematous uterine tissue of poorly compensated patients bleeds excessively and the risks of exsanguination and shock are superimposed upon those of cardiac exhaustion.

These patients require *constant* attendance, not only during labor, but for many hours thereafter. As has been mentioned previously, the majority of cardiac deaths in obstetric practice occur in the puerperium. For those patients with lowered cardiac reserve delivery should be by the method involving the least effort on the part of the patient. In competent hands cesarean section under local anesthesia is often the safest course. The patient should be propped up, no matter what the method of delivery, and delivered in a semi-recumbent position. This is especially important when mitral disease makes pulmonary edema a serious hazard. If delivery is by cesarean section, the patient should be sterilized at the same time; the

brief prolongation of operative manipulation adds little to the already grave risks. Further pregnancies must be avoided by some means. If sterilization of the woman or her husband is impossible or unwise, adequate contraceptive advice is urgently needed before these patients are discharged.

One aspect of medical therapy deserves special attention: the administration of oxygen. Oxygen is invaluable as a means of enhancing tissue respiration and improving the nutrition and strength of the myocardium. It has often been stated that "when cyanosis appears, oxygen therapy is indicated," but such advice is far too conservative. Early and prolonged inhalation of oxygen does no harm and may do immeasurable good in preventing cardiac default. It is hardly logical to expect efficient work from muscular tissue (both myocardial and myometrial) which must labor under conditions of inadequate oxygen tension. It must be recalled that even though there may be little gross anoxemia, nevertheless histanoxia (cellular tissue ischemia) is inevitable in circulatory failure. An elevated oxygen tension of the arterial blood is thus desirable.

The second stage of labor is the most exhausting. The physical effort is great and often protracted. Forceps delivery and/or episiotomy may reduce this burden. Ethylene is the anesthetic of choice from the internist's viewpoint. Ether may readily cause aggravation of the pulmonary edema associated with passive congestion.

Puerperal care is of the greatest moment in reducing the mortality and morbidity of cardiac damage. There need be no haste in removing the postpartum patient from the delivery room. She should be kept under close scrutiny for hours. Warmth, rest, oxygen and fluids are antidotal to postpartum shock. Hypodermoclysis of physiologic saline solution is somewhat safer than intravenous injection of fluids, unless the latter are administered very slowly. Where extensive blood loss has occurred several small (250 c.c.) transfusions of whole blood are desirable; not only do these

replace the loss in volume, but they offer replenishment of the reduced hemoglobin content of the blood. Oxygen does little good unless there is hemoglobin to carry it to the vital tissues. Oral ingestion of fluids, like parenteral administration, should be limited to small quantities taken frequently. These patients should never be dehydrated by restricting fluid. Such advice for the control of edema is mentioned only to be condemned. This applies to all edematous states, whether of circulatory<sup>15</sup> or renal origin.<sup>3</sup> But fluids must be given cautiously, a little at a time. Too rapid absorption of fluids may precipitate a rapidly fatal pulmonary edema.

#### SUMMARY

In such a brief résumé of the problems of heart disease in pregnancy it is possible to touch only briefly upon the more urgent aspects and to attempt to provoke an active curiosity about these questions. Generalizations are dangerous. There are very many variables which make each case a wholly individual problem in diagnosis, prognosis and management. The urgency of the clinical picture is frequently obscured by economic, emotional and sociologic factors. The functional capacity of the heart, as indicated by the response to stress on increased effort, remains the most reliable single criterion of prognostic import. The therapeutic management depends largely upon the prognosis, for the keystone of the whole structure of treatment of these patients is prophylaxis. To avoid cardiac failure, or postpone it as long as possible, is the objective in treatment of organic heart disease, irrespective of the anatomic lesion and regardless of pregnancy. Therefore the question of future pregnancies in either nulliparous, primiparous or multiparous women is an integral part of the problem. Preconceptional health evaluation and determination of functional reserves is the prime prophylactic measure. The right to bear children should never be denied without sufficient cause. The outlook may be greatly improved by intelligent

and whole-hearted coöperation between patient and physician during the prenatal period. Neglect and the assumption that the appearance of symptoms of failure will give sufficient warning for the institution of active therapy are dreadfully dangerous. The price of security is constant watchfulness.

Therapy to control the cardiac disorder must include application of all three of the cardinal principles of therapeutics: (1) etiologic therapy; (2) reduction of the physiologic burden of the injured structures; and (3) assistance to tissue nutrition and respiration. Of these three, the last is the most frequently neglected. It is the patient, not the disease, that is the physician's concern. Before giving any advice or making any decision, no matter how trivial or how serious, one must weigh the probable benefits against the probable detriments. If they are about equal, have the courage not to interfere.

#### REFERENCES

1. ADAIR, F. L., and STIEGLITZ, E. J. *Obstetric Medicine: The Diagnosis and Management of the Commoner Diseases in Relation to Pregnancy*. Philadelphia, 1934. Lea & Febiger.
2. STIEGLITZ, E. J. *M. Clin. North America*, 21: 281, 1937.
3. STIEGLITZ, E. J. *Abnormal Arterial Tension*. New York, 1935. National Medical Book Co.
4. JENSEN, J. *The Heart in Pregnancy*. St. Louis, 1938. Mosby.
5. LAMB, A. E. *Am. J. M. Sc.*, 187: 177, 1924.
6. SCHROEDER, C. *Arch. f. Gynäk.*, 150: 1, 1932.
7. BURWELL, C. S., STRAYHORN, W. D., FLICKINGER, D., CORLETTE, M. B., BOWERMAN, E. P., and KENNEDY, J. A. *Arch. Int. Med.*, 62: 979, 1939.
8. DIECKMANN, W. C., and WEGNER, C. *Arch. Int. Med.*, 53: 188, 1934.
9. Criteria Committee of the New York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart*. New York, 1939. New York Heart Association.
10. MACKENZIE, SIR JAMES. *Heart Disease and Pregnancy*. London, 1921. Oxford Medical Publications.
11. HERMANN, G. R. In Adair and Stieglitz. *Obstetric Medicine*.<sup>1</sup>
12. STIEGLITZ, E. J. *Am. J. Obst. & Gynec.*, 21: 26, 1931; *J. Missouri State M. A.*, 29: 505, 1932.
13. SODEMAN, W. A. *Am. J. M. Sc.*, 193: 121, 1937.
14. SMITH, F. M., GIBSON, R. B., and ROSS, N. G. *J. A. M. A.*, 88: 1934, 1927.
15. STIEGLITZ, E. J. *Ann. Int. Med.*, 6: 406, 1932.
16. JONES, H. W., and TOCANTINS, L. M. In *Obstetric Medicine*.<sup>1</sup>
17. HADEN, R. L. *Principles of Hematology*. Philadelphia, 1939. Lea & Febiger.
18. BICKEL, G. *Arch. des mal. du coeur*, 32: 769, 1939.
19. PARDEE, H. E. B. *J. A. M. A.*, 103: 1899, 1934.
20. STANDER, H. J., and KUDER, K. *J. A. M. A.*, 108: 2092, 1937.
21. STIEGLITZ, E. J. *Arterial Hypertension*. New York, 1930. Hoeber.



# ✓ ECTOPIC PREGNANCY\*

## A REVIEW OF 137 CASES

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NEW ORLEANS, LOUISIANA

NO chapter in gynecology is fraught with more interest and historical romance than that of ectopic, or extra-uterine, pregnancy. Woman, from the very beginning, was undoubtedly subject to the wayward migration and the aberrant implantation of a fertilized ovum with the consequent tragic sequelae; however, the writings of the ancients do not mention the condition. Sixteenth century investigators gathered reports of the occurrence of lithopedions, as well as of instances in which ulcers formed at or near the umbilicus or in the cul-de-sac, which upon dilatation permitted the escape of skeletal remains of a fetus along with putrid material. These cases comprised only that small group which we know today as primary ovarian or abdominal pregnancies, or those in which a tubal abortion has occurred and the fetus has been able to find a partially suitable site of nidation on the abdominal viscera with survival for varying periods of time. These early accounts do not take into consideration that large and important class of cases which we recognize today as early unruptured or ruptured tubal pregnancy. Diagnostic acumen and surgical skill had not yet developed to that point where the true pathology could be interpreted or proper treatment could be formulated.

Recognition that extra-uterine pregnancy is not a rare and bizarre condition paralleled the growth of abdominal surgery. Even in 1876, Parry warned the profession that, "Operative interference is condemned by the highest authorities upon the subject, and he who would subject a woman under these circumstances to the dangers of

gastrotomy would have to possess the courage of McDowell and his immediate followers." Parry collected 500 cases of ectopic pregnancy, the total number which had appeared in the literature up to 1876; of these 366 patients died and 163 recovered, a mortality of 67.2 per cent. It was not until almost the dawn of the twentieth century that operative interference was acknowledged as the treatment of ectopic pregnancy, for Lawson Tait, in 1883, was the first to perform the operation for ruptured tubal pregnancy, and although the first patient died, he correctly attributed his failure to faulty technique. Of the next forty patients only one died.

This present study comprises a review of all the cases of ectopic pregnancy which occurred at Touro Infirmary, New Orleans, during the years 1924-1936, inclusive. One hundred and forty-six histories were obtained, but nine of these were discarded because in five instances the patients were discharged without operation, and consequently, the diagnosis was not proved; and in four instances the operative notes and the absence of confirmation by the pathologist did not seem to justify the diagnosis of ectopic pregnancy. Three of these cases had been erroneously recorded as ovarian pregnancies, and the fourth was discarded because it did not seem to be a true interstitial pregnancy, for the pathologist reported a normally pregnant uterus.

A study of the statistics of ectopic pregnancy reveals an apparent increasing frequency of this condition. Older textbooks, written before 1900, give the proportion of extra-uterine to intra-uterine pregnancies in figures which vary from 1 in

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500 to 1 in 1200, whereas Wynne in 1919 reported 306 cases of ectopic pregnancy among 22,688 patients in the gynecologic clinic of Johns Hopkins Hospital, an incidence of 1.3 per cent of all gynecologic patients seen (Schumann).

Schumann found a ratio of one ectopic pregnancy to every 267 normal and still-born deliveries in the city of Philadelphia during the year 1918 (.38 per cent). To make allowance for those patients with ectopic pregnancy who are not admitted to hospitals, some of whom die at home under a mistaken diagnosis, and a few of whom recover without the aid of treatment, 10 per cent was added to the total reported cases, and, in consideration of the fact that all intra-uterine pregnancies do not go to term, and that approximately one abortion occurs for every four full term pregnancies, 25 per cent was added to the total number of births. The above figures, corrected in this manner, give a ratio of one ectopic pregnancy to every 303 normal pregnancies (0.33 per cent).

To obtain the relationship of extra-uterine to uterine pregnancy in New Orleans, 865 cases of ectopic pregnancy were collected, which had occurred in the seven hospitals located in the city during the years 1924-1936, inclusive. During these same years, 124,498 live births and 5,793 stillbirths, a total of 130,291 births, was reported. This reveals an uncorrected incidence of one extra-uterine to every 151 intra-uterine pregnancies (0.66 per cent). If these figures are corrected, according to the method used by Schumann, the incidence becomes one ectopic in every 171 pregnancies (0.59 per cent). This is the highest incidence of ectopic pregnancy which has ever been recorded in any locality.

It is extremely doubtful if the high incidence revealed by these figures represents an actual increase in the frequency of this condition. There are two facts to be noted in this connection: (1) the colored population of New Orleans is large and it is well known that the pelvis of the colored

woman is more subject to specific infection with its attendant damage to the adnexae than is that of the white woman; and (2) a large proportion of the work done in New Orleans' hospitals comes from out-lying sections where no hospitals exist, emergency cases being rushed to Charity Hospital and other institutions in New Orleans. It is very likely, moreover, that the apparent increase in incidence simply represents the increasing frequency with which the condition is diagnosed, and demonstrates a marked improvement in medical skill and education of the physician.

TABLE I  
ECTOPIC PREGNANCIES IN THE HOSPITALS OF NEW ORLEANS

(1924-1936 inclusive)

Charity Hospital.....	486
Baptist Hospital.....	83
Touro Infirmary.....	146
Hotel Dieu.....	52
Mercy Hospital.....	38
French Hospital.....	23
N.O. Dispensary.....	36
Flint-Goodridge.....	1

865 cases

BIRTHS IN THE CITY OF NEW ORLEANS  
(1924-1936, inclusive)

	Live Births	Stillbirths
1924	10,870	555
1925	10,239	526
1926	10,441	504
1927	10,463	542
1928	10,123	553
1929	9,383	401
1930	9,339	396
1931	9,207	321
1932	9,154	429
1933	8,532	407
1934	8,825	338
1935	8,959	403
1936	8,963	418
Total.....	124,498 130,291	5,793

The youngest patient in this study was 17 years of age and the oldest was 43 years. The largest number of cases, 65.2 per cent of the total, occurred in the decade 24 to 33.

Since implantation, conceivably, may occur at any point along the path followed

by the ovum in its migration to the tube, it follows that ectopic pregnancy may vary greatly in location. Such variations are common and are responsible for the classification of this abnormality according to the original site of implantation into three primary groups:

1. Ovarian
2. Tubal
  - (a) Ampullary
  - (b) Isthmial
  - (c) Tubo-ovarian
3. Interstitial

TABLE II  
AGE INCIDENCE

	No. of Cases	Per Cent
Not given	6	
17 years	1	
18 years	2	
19 years	3	
20-24 years	21	15.3
25-29 years	57	41.6
30-34 years	33	23.6
35-39 years	13	9.48
40-43 years	1	
	137	

Two other types of primary ectopic pregnancy, namely, cervical and abdominal, have been mentioned in the literature, and for the sake of completeness should be considered. Primary abdominal pregnancy would result if the ovum was fertilized while free in the abdominal cavity and was implanted upon any abdominal viscus. While this is theoretically possible, and while some few cases have been reported as such, the existence of abdominal pregnancy as a primary occurrence has never been proved and is extremely doubtful. Secondary abdominal pregnancies, although relatively infrequent, do occur and were the first cases of extra-uterine gestation to be recognized. Cervical pregnancy is occasioned by the implantation of the fertilized ovum in the cervix uteri, and although a few cases have been reported in which the cervix was undoubtedly the site of original

implantation, the condition probably arises most frequently from detachment of a normally imbedded ovum with subsequent reimplantation in the cervix. It seems more logical to consider it as a variety of uterine, rather than as an extra-uterine gestation.

The comparative frequency with which these primary forms occur cannot be accurately determined because, too often, the surgeon's notes make no reference to the location of the pregnancy and, as a rule, no attempt is made to trace a secondary ectopic pregnancy, when encountered, back to the primary form from which it originated. The published statistics of this condition, for these reasons, do not often mention the anatomic location. In analyzing the groups of cases reported in the literature, it can be seen that tubal pregnancy constitutes the large majority of cases, and that ovarian and interstitial pregnancy are both uncommon and occur with approximately equal frequency. In analyzing the 137 cases which form the basis of this study, very similar proportions are revealed.

Type	No. of Cases	Percentage
Tubal	134	97.9
Interstitial	2	1.4
Ovarian..	1	0.7

It is commonly believed by a large number of the medical profession that the right tube is more often affected than the left, and many reasons have been advanced to explain such an inequality. The most frequently advocated explanation is that the right tube is commonly damaged by acute appendicitis, and hence becomes a suitable site of ectopic gestation. The lateral dextrotorsion of the uterus is also claimed to explain the more common occurrence on the right side, but it is doubtful if any such relationship can be proved. Some authors have stated that the right tube is usually longer than the left, and that this increased distance, traversed by the

ovum on its way to the uterus, favored the development of pregnancy in the tube. This statement cannot be substantiated. Schumann is one of the few who expresses doubt concerning the greater frequency with which the right tube is involved and believes, from a review of his own statistics that but little variation occurs. Table III, from Schumann, supplemented by the present study and representing a total of 876 cases, reveals that a small series of cases may show a greater preponderance in either the right or left tube, but that a large group, as represented by the total, shows practically an equal distribution.

TABLE III

Author	Right Tube	Left Tube	Both Tubes
Oastler.....	54	46	2
Farrar.....	148	140	1
Bovee.....	28	31	0
Frank.....	23	29	0
Foskett.....	43	74	0
Williams.....	69	53	1
Present study.....	77	56	1
	442	429	5

Many factors of a varied nature can be held responsible for the production of ectopic pregnancy, but the difficulty lies in fitting any one of a number of theoretical or actual possibilities to the given case. In discussing this matter, it is best to consider separately the etiologic factors for the different forms.

Primary abdominal pregnancy has never been proved, and, since it exists chiefly as a theoretical possibility, it is not surprising that any explanation offered for its occurrence is purely hypothetical. It is thought that the presence of endometrial transplants, or of aberrant decidua, such as is quite commonly found in normal pregnancy, upon the peritoneal surfaces of many organs, might favor such an eventuality. It is a doubtful possibility and it is certainly best to consider both the occur-

rence and the explanation of primary abdominal pregnancy as outside the realms of practical thought.

Ovarian pregnancy is a proved possibility, and since Schumann, in 1921, reported a total of forty-three cases, the number is being added to with increasing frequency. For gestation to occur in this location, it is absolutely necessary for the ovum to be fertilized while it is still in the graafian follicle. It has been suggested by Leopold that a centrally located follicle may rupture into a superficial follicle, which has just extruded an ovum. This communication between the two must, perforce, be large enough to admit spermatozoa from the superficial follicle, and yet small enough to prevent the expulsion of the ovum from the deeper follicle. The existence of a perioöphoritis, with a resulting thickened tunica albuginea, could account for the stigma in normal ovulation meeting these requirements in size. Suffice it to say that the existence of ovarian pregnancy is definitely known, but its production is questionably explained.

Tubal pregnancy, by far the most common form, possesses a proportionately greater number of explanations and, from a mass of theory and clinocopathologic facts, the causative agents as listed by Schumann are generally accepted:

1. Obstruction of the tubal lumen from without.
2. Obstruction of the tubal lumen from within.
3. Anomalies of the tube, such as accessory ostia and congenital diverticula.
4. External migration of the ovum.
5. Decidual reaction in the tube.

Peritubal adhesions are the most common cause of obstructions located outside the tubal lumen. They frequently follow a perisalpingitis of extra- or intratubal origin, or an inflammation secondary to appendicitis, diverticulitis, or a general peritonitis following rupture of some abdominal viscus. Conservative operations for the relief of these very lesions may leave the tube more, rather than less, susceptible to

ectopic gestation. Giles, from a group of 125 cases, reported that 24 per cent of women who became pregnant after conservative surgery of this type had extra-uterine gestations. Even the correction, by suspension, of retrodisplaced uteri may, in the absence of tubal pathology, predispose to this development, as was revealed by P. W. Siegel, who found that 15 per cent of his seventy-three patients ectopically pregnant became so after suspension of the uterus. Other gynecologic operations apparently have little influence in this direction. The presence of a tumor in some neighboring tissue may also obstruct the tubal lumen from pressure and favor implantation of the ovum. Plastic operations upon the tube, performed either to produce sterility or to relieve it, frequently are followed by ectopic gestation. Spontaneous torsion of the tube, though a rare occurrence, can obstruct the lumen of the tube and represents a factor which should be included in this group. Numerous cases proving the occurrence of all these factors have been reported.

Salpingitis, particularly of gonorrheal origin, is the morbid process usually responsible for obstruction of the tubal lumen from within. Williams found evidence that an inflammatory reaction had preceded ectopic pregnancy in all his specimens. When both tubes were removed, these changes were proved microscopically to be bilateral, and diverticula were found not only in the pregnant tube but in the opposite one also. Other factors, not inflammatory in origin, which can obstruct the lumen from within, can be mentioned. Katz believes that the cyclical changes demonstrated in the tubal mucosa during menstruation and pregnancy can result in a heaping up of the epithelial cells on each other to such an extent that mechanical obstruction may result. Rubin has also shown the existence of spasm in the tubal musculature, and has revealed that pressure, much greater than normal, is necessary to overcome such resistance. Such a spasm, with an absence of normal peristal-

sis, could readily interfere with the progression of the ovum.

Diverticula, similar in all respects save in inflammatory reaction to those produced by salpingitis, have been commonly found in the Fallopian tubes. Their existence is predicated upon an abnormality in the embryologic canalization of the lumen. Accessory ostia and accessory tubes likewise represent pockets in which the ovum may be trapped. A persistence of fetal characteristics, i.e., excessive length and more numerous convolutions, increases the distance to be traversed by the ovum and may also interfere with tubal peristalsis. Both of these factors predispose to ectopic pregnancy.

Increase in the size of the ovum, rather than narrowing of the tubal lumen, could prevent the ovum from reaching the uterine cavity. Such an occurrence can be explained by external migration of the ovum. This term is used to describe the wandering of a fertilized ovum from one ovary across the pelvic cavity to enter the tube of the opposite side. The increase in size of the ovum results from growth during the greater length of time required for such a journey. Cases have been described in which no other mechanism, aside from external migration, could explain their occurrence. It is not, however, believed to be a frequent factor.

The occurrence of a decidual reaction in the tube is believed by many to be the most important contributory factor, for it would invite attachment and implantation by any ovum with which it came into contact. Such a decidual reaction can result from the presence of endometrial transplants in the tube or from an actual decidual response in the tubal mucosa. Döderlein and Herzog have reported a case of ectopic pregnancy located in an adenomyoma of the uterine wall, proving beyond all doubt the existence of this factor. Actual decidual response in the tubal mucosa has been demonstrated to occur in normal pregnancy by many investigators. It is regarded by some as an evidence of functional degener-



acy with reversion to a lower type. Frankel and Schenck have found decidual tissue to be present in the tube of 87.5 per cent of specimens of ectopic pregnancy which they have examined, and Kermauner has demonstrated decidua in the tubes of 15 per cent of a series of normal pregnancies. These findings suggest that some other factor other than tubal obstruction may play the essential rôle. It is probable that tubal obstruction must occur in association with a complementary influence, which would create a favorable soil for implantation, in order for ectopic pregnancy to result. A decidual response in the tubal mucosa can well answer this purpose.

An attempt to determine the etiology of the 137 cases collected for study was hindered by the scarcity of information recorded in the hospital histories. Only those factors mentioned in the pathologic report were found useful. The microscopic study of those cases reaching the laboratory revealed the presence of salpingitis, a definite etiologic factor, in twenty cases (14.6 per cent). A review of the operators' notes located three cases which may possibly have resulted from external migration of the ovum. A decidual response in the tubal mucosa was rarely noted.

In considering the eventual termination of any extra-uterine pregnancy, it should be remembered that three essential possibilities can occur: (1) early death of the fertilized ovum with complete resorption; (2) development of the fetus to term, or else to an advanced state, in its site of original occurrence, with the possibility of delivery by laparotomy, or if retained, death followed by such terminal changes as suppuration, skeletonization, lithopedion formation, or saponification; (3) rupture. If rupture results, three developments may take place: (1) the embryo may die; (2) the embryo may become reimplanted and continue to grow; (3) the placental attachments may survive at the primary site, and the fetus, its position changed, continues to develop.

Regardless of the manner in which rupture occurs, and regardless of the variety of ectopic pregnancy involved, hemorrhage into the peritoneal cavity of the mother is almost universal and is frequently copious. If this hemorrhage is very profuse and rapid, exsanguination of the patient prevents the occurrence of further changes. However, if the bleeding occurs slowly and in smaller amounts, especially if the lesion is a tubal abortion, the blood may gravitate into the cul-de-sac and become partly organized. The presence of blood in the peritoneal cavity incites an irritative, plastic, aseptic peritonitis, and the collected blood becomes walled off by adhesions, forming a hematocele. Hematocele represents a favorable termination of ectopic pregnancy, for it predicates the passage of sufficient time for hemorrhage to have ceased and the chances of exsanguination to have passed. It is not without its dangers, however, for the collected clot and free blood may become infected and form a pelvic abscess.

	No. of Cases	Ruptured	Unruptured	Not Stated
Right tube	77	56	20	1
Left tube	56	36	15	5
Bilateral	2	2	0	0
Ovarian	1	1	0	0
Cornual	1	0	1	0
	137	95 69 4 per cent	36 26 2 per cent	6 4 4 per cent

The scarcity of information in the hospital records, particularly in the surgeons' notes, is again revealed when an attempt is made to analyze the present study as to termination. Frequently, the condition of the tube at operation was not described, and hence, it was impossible to determine whether tubal abortion or tubal rupture had taken place. One abdominal pregnancy, secondary to tubal rupture, occurred in which the embryo had become reimplanted upon the anterior wall of the

rectum. For the whole series, it was possible to divide the cases into ruptured and unruptured groups only. Those cases classed as unruptured were, in all probability, tubal abortions, although the information furnished was not sufficient to justify calling them so.

Before rupture occurs, no symptoms exist aside from those common to early uterine pregnancy, such as amenorrhea, nausea, vomiting, soreness of the breasts, and frequency of urination. Occasionally, a vague sensation of discomfort or soreness may be noted upon the affected side. Amenorrhea is not always constant, but when present, usually leads the woman into a false belief that she is normally pregnant. Vaginal examination before rupture may reveal a slight softening of the cervix and perhaps a slight enlargement of the uterus. However, changes in the size and consistency of the affected tube are indefinite and of little specific diagnostic significance.

The absence of unusual symptoms is responsible for the fact that extremely few women consult a physician during this period, and the lack of any characteristic physical signs results in a failure correctly to diagnose those cases which do present themselves. No clinical alterations occur in the blood or urine, and, although the Friedman test is positive, an early normal pregnancy is suspected. The diagnosis of an unruptured ectopic pregnancy during early development is attended with the same luck which blesses the golfer who scores a hole-in-one.

When rupture does occur, the history is extremely important if a correct diagnosis is to be made. Usually, there will have occurred a period of amenorrhea of one month's duration or longer, followed by "spotting," or even by vaginal bleeding of a more frank nature. There are two important characteristics of this bleeding which should be noted: it occurs at a period which is not in rhythm with the regular menstrual cycle, and it is most often of a dark brownish black color.

A period of amenorrhea does not always preëxist before rupture. No period may have been missed, but it may have been delayed a few days, or careful questioning will reveal that the last menses were very scanty and not entirely normal. This "irregularity" of menstruation, whether associated with amenorrhea or not, is one of the most important and frequent symptoms. Rarely, ectopic pregnancy may proceed to rupture without any noticeable menstrual disturbance, but in such a case there is always a question of the care with which the history was taken.

A history of amenorrhea preceding the onset of symptoms is recorded in seventy-two of the present series of 137 cases (52.8 per cent). The information is vague on this point in many of the histories. Where a provisional diagnosis of some other condition than ectopic pregnancy was given, there is very seldom mention of a period of amenorrhea. A history of abnormal vaginal bleeding was recorded in 111 cases (81 per cent). This bleeding continued until the operative day in some cases and was intermittent in others. Five patients expressed a belief that they had passed the products of pregnancy. In ten cases, a dilatation and curettage had been performed previous to admission; in twenty-two, curettage was performed at the time of operation. Throughout the series, abnormal bleeding is often reported as a normal menstrual period. The information on these two symptoms, amenorrhea and bleeding, is more confusing and less accurate than on any other phases of the syndrome. There were twenty-six patients in whom no history of bleeding was recorded. Fifteen of these were in shock at the time of admission. Careful inquiry, after operation, might have altered this finding.

Pain in the pelvis, usually recurring in a fairly definite cycle, is the next most important point in the history. It may be sudden, severe, and lancinating in type, or may, in its incipency, resemble menstrual cramps. An analysis of the frequency of the various

symptoms in the series revealed that only six patients suffered no pain. The absence of pain was definitely stated in the history of five of these, and, in one, pain was not mentioned as a symptom. In the majority of cases where rupture occurred, pain was sudden and severe, but in some instances was preceded by cramps in the lower abdomen. Occasionally, pain was the initial symptom and occurred without relationship to an irregularity in menstruation. Radiation of pain to the thighs, back, and chest was noted. Shoulder pain occurred in thirteen cases. The frequency with which rupture occurs in the bathroom is a finding that impresses the investigator of a series of cases. Intraabdominal pressure is increased by straining during urination or defecation, and this force applied to a tube distended to its fullest extent results in immediate rupture.

The onset of sudden pain was accompanied by fainting or by several fainting spells in nineteen cases, and thirty-one complained of a feeling of faintness or weakness, which made a total of fifty cases with symptoms of syncope (36.4 per cent). Forty-one patients (29.9 per cent) were in a state of shock at the time of operation, and in most instances this meant at the time of admission. There were a few patients upon whom operation was delayed, in the absence of the correct diagnosis, who went into shock during their hospital stay.

Nausea, or both nausea and vomiting, were present in fifty-five cases (40 per cent). As a rule, it began with the onset of pain and was not noted as an accompaniment of the pregnancy until the acute symptoms manifested themselves.

Cullen's sign was recorded in only one case, although it was looked for as a diagnostic sign in many instances.

Upon physical examination, the most universal finding was tenderness in the lower abdomen, which was present in 111 cases (81 per cent). Both quadrants of the lower abdomen were equally painful in forty-four cases (32 per cent). Tenderness

was more marked on the right in forty-eight cases (35 per cent), and on the left in nineteen cases (14 per cent), although in some it was present in a lesser degree on the opposite side also. In twenty-six cases (19 per cent), there was no tenderness in the lower abdomen. Eight of these were in shock at the time of examination, and in eleven the tube was unruptured. There were several patients who complained of tenderness in the gall-bladder region as well as in the lower abdomen. Tenderness was present very often in the absence both of rigidity of the abdomen and of a palpable mass.

Rigidity was found in only fifty-seven cases (41.6 per cent). In some, the rigidity was slight, and in many was evident only upon deep palpation. In others, the whole abdominal wall was tense and "rigid as a board." The tube was ruptured in all but six of the fifty-seven cases with rigidity; in three of the six, there was only slight rigidity; in five of the six, a mass was also palpable.

In fifty-four of the 137 cases, a mass was palpable. It was located in the right lower quadrant in twenty-eight cases (20 per cent); in the left lower quadrant in fourteen (11 per cent); in the posterior cul-de-sac in six (4.5 per cent); in the midline in five (4 per cent); and occupying the whole pelvis in one case (0.7 per cent).

Examination of the blood, after rupture, reveals changes which are dependent upon the amount of intraperitoneal hemorrhage. Recent profuse hemorrhage was shown by Farrar to cause a marked leucocytosis, whereas, in milder types, the leucocyte count may show no change. The red cell count and hemoglobin are directly related to hemorrhage and fluctuate accordingly. The urine, scanty in amount because of the loss of body fluids, shows no changes unless hemoglobinuria, resulting from intraperitoneal hemorrhage, is demonstrated. The Friedman test may be positive or negative according to the viability of the trophoblast.

The statement is often found in the literature that a relative sterility of long duration usually precedes the development of ectopic pregnancy. This is not borne out in the present study, for sixty-two of the 137 women were found to have been previously pregnant. (Table iv.) Of these sixty-two women, twenty-three had had three or more children; no statement was made in forty-four histories.

TABLE IV  
PREVIOUS PREGNANCIES IN 62 CASES

No. of Cases	No. of Pregnancies
23	1
16	2
7	3
4	4
4	5
5	6
1	8
2	9
—	—
62	38

In sixty-five of the 137 cases (47.2 per cent), the diagnosis of ectopic pregnancy was correctly made. In thirty-two cases (23.5 per cent), the diagnosis was thought to be ectopic pregnancy or some other condition. In forty cases (29.3 per cent) the diagnosis was entirely erroneous. If these cases, in which the possibility of ectopic pregnancy was weighed against some other condition, are added to those in which the diagnosis was unequivocally correct, the resulting percentage, 70.7 per cent, of accurate diagnoses parallels closely that found by other investigators.

The dictum that all cases of ectopic pregnancy should be subjected to operation as soon as possible, regardless of the patient's condition, should be the unvarying rule for every physician who makes such a diagnosis. The inability to foretell the result of an internal hemorrhage, and the suddenness with which rupture can occur, are factors which make this rule just as applicable to the woman who with an early unruptured tubal pregnancy has no symptoms as it is for the patient in grave shock from excessive bleeding. There is no

such thing as expectant treatment for extra-uterine gestation because the prognosis becomes more serious the longer operation is delayed. Hunter Robb's statement, based upon experimental surgery in dogs, that intra-abdominal hemorrhage is seldom, if ever, the cause of death, cannot hold water when contrasted with the statistics collected by Parry. Parry collected the records of 500 cases of ectopic pregnancy with 386 deaths. Of the total number of deaths, 174 (52.8 per cent) resulted from hemorrhage following rupture. Of these 174, the duration of life after rupture is mentioned in 113. Of these 113, 71.7 per cent were dead within twenty-four hours, and only 13 per cent were alive after forty-eight hours. These figures alone should impress everyone with the necessity for haste in the treatment of this condition.

No time should be wasted before surgery by transfusion or infusion in an attempt to rally these patients. Such procedures can be accomplished during the progress of an operation, and the patient will benefit greatly from the time saved. Cases can always be recalled in which death occurred, without operation, while valuable time was lost in a search for blood donors, or in a period of "watchful waiting" for the general condition of the patient to improve. On the other hand, it is customary to note a marked improvement in the pulse of a gravely shocked patient as soon as the bleeding vessels have been ligated at operation, despite the fact that no fluids or stimulants were administered. It is well to repeat that the time for the administration of fluids is during, or after, the control of the hemorrhage by ligature.

The extent of the operative procedure is limited by the judgment of the surgeon and by the patient's condition. If hemorrhage has been severe, its control by removal of the affected tube is all that can be asked. If the blood loss has been slight, and the patient's condition warrants it, the remaining tube should be carefully inspected and, if evidently diseased, removed. The extravasated blood is best left in the patient's

abdomen for eventually it is absorbed and attempts to remove it increase the length of the operation. No more surgery should be practiced upon the victim of a ruptured ectopic pregnancy than is absolutely necessary to insure a primary postoperative recovery. He who under such circumstances, incidentally removes the "chronic appendix," or suspends the uterus, or explores the abdomen after removing the affected tube will increase his operative mortality by a great percentage.

In a certain number of cases, ectopic pregnancy recurs in the remaining tube. Smith studied 1,608 cases operated upon by members of the American Gynecological Society and found fifty-eight repetitions

(3.6 per cent). In five of the 137 cases (3.6 per cent) from Touro Infirmary, a previous ectopic pregnancy had occurred. The percentage incidence in these two series is the same.

Three deaths occurred in the series of 137 cases. This represents a mortality of 2.18 per cent, which compares most favorably with that of 7.7 per cent reported by Schumann. Mortality, in any condition, is dependent upon the skill of the physician, but it is estimated that the average mortality in the better hospitals will be 4 per cent, or under. The operations in the present study were performed by forty-three different surgeons and this fact precluded the possibility of follow-up by this investigator.



IN 1937 . . . fetal and neonatal deaths aggregated 142,500. This is more than the number of deaths occurring among individuals in the age group of five to twenty-nine years (132,000) and is approximately 10 per cent of the total deaths for all ages and all causes (1,450,000).

From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

# THE TREATMENT OF ABORTION\*

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THE etiology of abortion is very important in the prevention and treatment of this condition. Improved social and economic conditions and education in contraception will reduce the number of self-induced and criminal abortions, with the associated high rate of invalidism and mortality. In a review of 1,000 abortions, 65 per cent of induced abortions were in single women and 35 per cent in married ones. The intelligent woman will have pelvic pathology corrected before conception and even before marriage. Pregnancy is not likely to continue in a uterus that bleeds profusely or irregularly, in one that contains a submucous or intramural fibroid to interfere with development of the placenta or the nourishment of the fetus, or where there is a hyperplasia of the endometrium preventing proper nidation of the ovum and suggesting ovarian hormone disturbance.

At the first prenatal visit, the patient should be asked to coöperate in the prophylaxis of abortion. She should be impressed with the necessity of avoiding violent exercise, excessive fatigue, highly emotional states, long automobile rides over rough roads and sexual intercourse during the first trimester. Previous history of abortion, in the absence of well defined cause, suggests the following treatment: bed rest, sedatives, particularly barbiturates, at the time of an expected period, and again at six, eight and twelve weeks' gestation.

Spotting with a dark brown, odorous irritating discharge, without cramps is common in early pregnancy, before the womb is entirely filled and the space between the reflexa and vera is closed. At this time the endometrium that is not covered completely is very vulnerable and

is apt to bleed from any condition that causes excessive pelvic congestion such as constipation, fatigue, sexual intercourse, and emotionalism. The same type of bleeding, with the addition of vague cramps or more active bleeding with or without contractions indicates that *abortion is threatened*. Cramps in the lower abdomen without blood are difficult to differentiate from colic, but the absence of diarrhea, constipation or meteorism and urine tests negative for pus or blood indicate the necessity of strict treatment. One must consider, in the absence of cramps, the possibility of the origin of bleeding from an erosion or polypus of the cervix.

Essential treatment for threatened abortion consists of (1) absolute bed rest; (2) ice-bag to lower abdomen; (3) raising the foot of the bed 8 to 12 inches; (4) no cathartics or enemas for three days, then oil retention enema; (5) pelvic examination, through rectum only, if absolutely indicated. (6) sedatives: phenobarbital  $1\frac{1}{2}$  gr. b.i.d., codeine  $\frac{1}{2}$  gr. with aspirin gr. 10 if pain is present, however mild; morphine, except in large doses, may stimulate contractions; (7) thyroid, if there is evidence of hypothyroidism; (8) wheat germ oil, 2 to 6 c.c. daily in capsules of 1 c.c. each; (9) progesterone 5 to 15 mg. daily. This treatment should be continued until the cramps and bloody discharge disappear. Determine the latter, if not visible, by inserting a cotton probe into the vagina.

Bed rest should continue for at least five days after bleeding has ceased. The treatment of threatened abortion is deterrent while that of inevitable and complete abortion is provocative. About one-third of threatened abortions will recur after all symptoms have subsided. Unfortunately

\* From the Gynecologic Service, Minneapolis General Hospital.

there are no definite clinical signs to show that a recurrent threatened abortion will go to term. There is evidence that vitamin E is concerned with thyroid activity, and has a relationship to normal pituitary and ovarian function. Doses of wheat germ oil containing vitamin E are given in amounts as high as 15 c.c. daily. This dosage does not seem advisable since the ill effects of hyper-*vitaminosis* have been proved for some other vitamins, particularly vitamin D.

Progesterone prevents uterine contractions by opposing the estrin effect of sensitizing the uterine muscle.

Completed abortion is indicated by a closed cervix, more or less complete reduction of the bloody discharge, decreased size and greater firmness of the uterus and absence of pain in the lower abdomen. It is definitely established if the complete ovum is observed. If bleeding recurs after the use of ergot or if bright red blood reappears, the abortion is probably not complete. The treatment is bed rest of four to ten days, depending upon the duration of the pregnancy.

Inevitable and incomplete abortion is termed febrile or afebrile if the highest daily temperature is above or below 100.4°F., respectively. Each requires different treatment, expectant in febrile cases and active in afebrile, allowing an interval of five days of normal temperature to elapse before evacuation of the retained secundines.

Excluding cases of endogenous infection, febrile abortion under three months gestation is undoubtedly self or criminally induced. If, during the waiting period, the abortion has not completed itself, evacuation is indicated, the method used depending upon the amount of cervical dilatation and the month of gestation. In febrile cases with severe hemorrhage, immediate evacuation should be performed and the uterus should not be packed, if bleeding seems to be controlled.

The essentials in the treatment of incomplete afebrile abortion are: (1) ice bag to lower abdomen; (2) quinine not

exceeding 15 gr.; (3) pituitary extract 5 units every six hours or fluidextract of ergot 10 minims t.i.d. for three days, to be repeated if bleeding recurs or incompleteness is suspected (the equivalent may be given in ergotrate, i.e., half of a 5 mg. tablet t.i.d. for a maximum of three days); (4) 1000 c.c. of 5 to 10 per cent glucose solution in normal saline, in emergency, for shock, profuse blood loss, or in septic cases with reduced food intake; (5) blood transfusion, 500 c.c., as indicated.

In febrile cases the following are added: (6) sulfanilamide. If intra-uterine or blood culture is not practical it may, nevertheless, be advisable to give the drug in tablet form, 15 gr. every four hours the first day, 10 gr. every four hours for the second and third days, after which, the concentration is maintained at 10 mg. per 100 c.c. of blood. If this determination is not available, give 40 gr. on subsequent days up to five to seven days. Discontinue for a few days and repeat if lack of improvement warrants. A rise in temperature and cyanosis may occur, but they are not important; Nausea of varying degree may necessitate subcutaneous administration which is given immediately and slowly by drop method in the anterior thigh. This solution is prepared by dissolving 0.8 Gm. of the drug in 100 c.c. of boiling normal saline solution which is then cooled to body temperature. It deteriorates on standing.

Five grains of sodium bicarbonate is given with each oral dose to limit the nausea and prevent acidosis. No other drug is administered, especially not sulfates, during treatment and for three days after treatment is discontinued. Hemoglobin, leucocyte and red cell counts are taken before treatment and daily after treatment. Hemolytic streptococcus infection accentuates the depreciation of the blood. Low values in a kidney function test contraindicate this treatment. Urinalysis should be done daily. Blood in the urine indicates cessation of treatment. The drug is stopped if acute hemolytic anemia, leucopenia or sulfhemoglobinemia develops. A transfusion

is given before treatment if hemoglobin is below 70 per cent (Sahli). Preliminary blood grouping is desirable. If anemia alone develops and can be controlled by transfusion, treatment may be continued. In the absence of the more complicated laboratory procedures, one will have to depend upon objective and subjective signs and prophylactic transfusion.

Chemotherapy has been limited to the use of sulfanilamide which has selective action and has been used successfully in gonococcus, staphylococcus, hemolytic streptococcus and *Clostridium Welchii* infections. The last two are usually fatal, especially if blood culture is positive. However, there have been miraculous cures, particularly when the infection is unmixed and treatment is instituted early. The dangers from sulfanilamide are minimal if proper precautions are taken. If it is not tolerated by mouth, parenteral administration is indicated.

Transfusion is very valuable in small amounts frequently given (200 to 300 c.c.).

**Surgery.** The retained products are not evacuated until at least five days of normal temperature have elapsed. The only exceptions to immediate evacuation in febrile cases are: (a) severe or prolonged profuse hemorrhage; (b) dilated cervix, filled with decidua, preventing drainage. In the first case evacuation should be complete, with packing for twenty-four hours, if necessary, to control bleeding.

Fever may be due to sapremia rather than infection; the chills and temperature will return, immediately, to normal. Clinically, the patient's appearance does not seem to justify diagnosis of infected abortion.

A pelvic abscess in the cul-de-sac may be emptied by posterior colpotomy. Posterior parametritis may be mistaken for an abscess. Incision is useless and dangerous. An intraligamentous abscess may be drained, when it rises above the pubis, by incision parallel to Poupart's ligament.

Of our 1,000 cases, 26 per cent were febrile. All were treated conservatively,

giving a mortality of 1.9 per cent or a corrected mortality of 1.3 per cent, if the patients entering the hospital moribund are eliminated. Expectant-active treatment is justified by the lower mortality, fewer disabling sequelae and the recognition of established surgical principles. The temperature reaction of pelvic examination indicates the disruption of the leucocytic barrier; invading the uterus at the improper time often determines a fatal issue, as many a consultation recalls.

**Missed Abortion.** Taussig estimates that one-tenth of the spontaneous are missed abortions. Litzenberg recommends evacuation as soon as the diagnosis is made. Quinine and pituitary extract, after sensitization of the uterus with repeated doses of 20,000 units of estrin, may cause proper uterine contractions. Failing in this, the cervix may be softened by packing and in advanced cases, the bag, in early cases, graduated dilators, will open the womb. Then evacuation is carried out with ovum or sponge forceps, followed by packing for the usually free hemorrhage.

**Habitual Abortion.** Evidence is available that habitual abortion, in the absence of general disease or local pathology, is due to a disturbance of estrogen production and the prolan-progesterone mechanism of pregnancy. The values of these, in blood and urine, vary at different periods of gestation and although the minimal requirements for successful continuance of pregnancy are as yet not definitely known, the new treatment of threatened and habitual abortion seems to show results.

Endocrine assays by Brown, Hendry and Venning in twenty-five cases of habitual abortion indicate that alternate daily doses of less than 5 mg. or 5 rabbit units of progesterone are not likely to have much effect. Abortion is most likely to occur at the time the necessary gestational hormones are transferred from production in the ovary to the placenta. Since this period is variable and assay is not within the province of many, at least 5 mg. of progesterone should be given daily or on alter-



nate days, with increased dosage in cases of threatened abortion. Administration should begin a few weeks before the time of the previous earliest abortion. If abortions in the individual have occurred early and late, the treatment may be interrupted in a portion of the interval.

The well known responsibility of hypothyroidism in sterility suggests the use of thyroid extract in habitual abortion, with dosage determined by symptoms and basal rate.

An additional probable factor in habitual abortion, vitamin E deficiency, can be provided for in the form of wheat germ oil, 3 to 6 c.c. daily in capsules of 1 c.c. each.

*Technique of Abortion.* The methods used at the Minneapolis General Hospital are as follows:

1. If dilatation is necessary, graduated dilators are used, in the early months, a Vorhees bag in the later months. A long and firm cervix is not easily dilatable; a gauze pack for twelve to twenty-four hours will soften it sufficiently to insure dilatation with a bag.

2. Up to the fourth month, evacuation is performed with ovum or sponge forceps after determination of the position of the

uterus and the length of the cavity. Measurement is done with the same instrument, which because of its blunt extremity, is not likely to perforate the uterus.

After the third month, one or two fingers are used to separate the placenta, at the same time pressing the uterine wall to the fingers from above. Precede this procedure with 1 c.c. of pituitrin hypodermically.

3. The curette, a blunt one, is used only in cases of long standing with fairly firm fundus.

4. Packing is usually unnecessary and is to be avoided except for hemorrhage; however, it is nearly always necessary after evacuating a missed abortion.

#### SUMMARY

1. Treatment is given for various types of abortion except therapeutic.

2. Recent advances in treatment comprise the use of sulfanilamide in certain infected cases. Vitamin E and progesterone are administered in threatened and habitual abortion.

3. Conservative treatment is stressed.

4. Technique of operative procedures is indicated.



# THE HEMORRHAGES OF LATE PREGNANCY AND LABOR: PLACENTA PREVIA AND ABLATIO PLACENTAE

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## INTRODUCTION

IT is indeed fortunate that placenta previa and premature detachment of the placenta are such infrequent complications of the puerperal state, for, while they severally occur but once in 500 advanced gestational periods the resultant deaths constitute approximately 7 to 10 per cent of all puerperal deaths. The lethal dangers being so great, it behooves all obstetric attendants to become thoroughly conversant with every diagnostic detail of these two emergencies, so that prompt and appropriate therapy may be instituted. It is imperative that the attendants be facile in combating these catastrophies, or possess the moral courage to transfer the responsibility to someone so qualified.

Placenta previa and ablatio placentae have a number of attributes in common, as well as some which are vividly dissimilar. Their convergent details lead to diagnostic uncertainty, even confusion; their diversities are so dramatically distinctive that he who runs may read.

*History.* The tracing of the development of the knowledge of the one may not be dissociated from the other, for both have a common origin and course. The Hippocratic teaching that nature had so generously provided a nesting place in the fundus of the uterus that invariably the placenta was there attached was considered gospel long over a millenium and a half. During all this time it was held that the hemorrhage of advanced pregnancy was due to a fundal separation, placental prolapse, and possible birth before the egress of the child. Even when the refutations of keen observers of the early sixteenth to eighteenth century became known, many still believed that Hippocrates was right and even when

the truth did prevail many vehemently maintained that the normally situated placenta could not separate in pregnancy.

Paul Portal (1664) graphically described placental presentations but no credence was accorded to the new teaching. Gottlieb Schacker (1709) ably reported the post-mortem findings in a woman dying from a premature placental detachment where the uterus was filled with blood. Bernard Albinus (about 1750) recorded a similar example which he discovered by autopsy. Giffard (1734), Smellie (1766), Levret (1766) added certain basic principles to our knowledge of placenta previa. Rigby (1776) first gave a clear clinical and anatomic differentiation of placenta previa from premature detachment. We may doubt the accuracy of some of his diagnoses, but we must concede that he did see clearly the segregation of hemorrhages into the two definite types. He denominated a placental presentation as *unavoidable*, and the other as *accidental*.

A. C. Baudelocque (1804), in his thesis on uterine hemorrhages, lucidly described cases of placental detachment wherein the uterus was distended with blood. Mme. Boivin, in discussing his presentation, denied the possibility of such occurrences as he described, for neither she nor Mme. La Chapelle had seen such in over 42,000 labors. Hodge of Philadelphia took the stand of Mme. Boivin. As late as the last decade of the past century Lusk and Cazeaux and Tarnier dismissed the subject with scant paragraphs.

Tanner (1851) presented a paper based upon a few cases culled from the literature; Hicks (1860), Goodell (1870), and H. R. Storer (1892) supplemented these, until the last had some 140 cases assembled. The

writer (1901) collected 198 cases not previously compiled with two reports of original cases in a paper entitled "Ablatio Placentae." Up to this time, while certain British hospitals, notably the Rotunda of Dublin, annually included cases of accidental hemorrhages in their statistical reports, comparable in number to that obtaining for previa, numbers of large American hospitals with large obstetric services failed to record a single instance. To this day, most of the federal and state vital statistics concerned with puerperal mortalities enter the deaths from premature detachment among "other puerperal hemorrhages," though they are almost as numerous as deaths from placenta previa.

*Etiologic Resemblance.* It is generally believed that endometritis is a fruitful contributory factor in the preparation of the lower uterine segment for a previal implantation. Premature detachment has been accorded the same etiologic influence, either as a contributory or direct association.

*Source of the Hemorrhage.* The two entities have a common origin for the bleeding—from the opening of uterine sinuses; in one the blood losses result from a separation of a viciously inserted placenta, in the other, from a normally implanted one. The hemorrhage in both may be initiated by some casualty. The hemorrhage in frank previas is almost invariably "silent." Almost never is the pain or discomfort intrinsic to the condition. The bleeding in premature detachment, on the other hand, produces an array of objective and subjective signs which vary with the placental location, the suddenness and extent of placental separation, and the amount and the rapidity with which the effused blood accumulates within the uterus. The line of demarcation between a high lateral previa and a low normally implanted placenta may not be clinically demonstrable: the lower rim of the respective types may become detached, and the escaping blood may arouse no symptom, or if the extravasated blood be restrained for

a period, there may be vague to marked subjective disturbance.

*Nomenclature.* The terms placenta previa, placental presentation, and unavoidable hemorrhage are so lucid they carry no false or ambiguous interpretations. However, the titles adopted for premature detachment of the normally situated placenta mostly connote erroneous concepts of the etiology, or of the symptomatology. Accidental hemorrhage carries the implication of a mishap or traumatism, and the majority of the writers previous to the dawn of this century accepted the name as such, although Rigby was most emphatic that he meant the term to cover fortuitous circumstances. The old literature teems with case reports wherein overt or specious traumatisms were the cause—and when these were not pronounced or occurring imminently in relation to the hemorrhage, the attendants avidly sought, and found, some sort of jolt long antedating the catastrophe which was duly assigned as the "cause." A. C. Baudelocque (1804) associated the word "concealed" with Rigby's "accidental"—still further befogging the title. Very few cases are reported where from the moment of occurrence to the time of delivery there is no external evidence of blood loss, since sooner or later patent hemorrhage will supervene. *An overt hemorrhage is never a concealed one.*

That the atmosphere might be clarified, the author sought counsel from a professor of Latin and Greek, explaining the picture of premature detachment: He asserted that the analogy of *ablatio retinae* justified the name *ablatio placentae* or *placenta ablata*—the placenta is torn away. Therefore, the writer has used this term as the generic description for premature placental separations, due to any cause.

De Lee (1901) suggested that the condition should be christened *abruptio placentae*, but *abruptio* is incorrect in its premises as not more than one detachment in ten has a sudden, violent or tumultuous onset. The term thus carries erroneous implications of the symptomatology. The

title of this paper, *Hemorrhages in Late Pregnancy and Labor*, is misleading in an anatomic and chronologic sense, as both

placenta previa and ablatio may be the cause or the comitant of early abortions or miscarriages.

## PLACENTA PREVIA

A previa obtains when any portion of the placenta, large or small, dips into or below the potential site of the retraction ring. This means that part of the placenta is implanted in the lower uterine segment or the dilating part of the uterus. It is unfortunate but true that obstetricians have not agreed upon a common grouping of the degrees of placental presentations, or upon a conception of what the designating names imply, or upon the anatomic conditions which must exist for the diagnosis of the extent of placental presentation. According to the caprice of the individual writer two or more of these terms are employed—central, complete, incomplete, partial, marginal, and lateral.

The degree of the previa is interpreted at the time of the diagnostic examination, whether the os be undilated or widely opened. However, it should be determined by the correlation of the placenta to its site before any effacement or dilatation has occurred. Thus the attendant, when belatedly examining the patient, should endeavor to envisage conditions as they were originally, not as he finds them. Effacement and passive dilatation are present in nearly all women as labor is imminent. When there is a placental presentation, effacement produces new relations of the placenta and its site which may be accomplished only by a tearing of their juncture. The hemorrhage is merely the manifestation of the placental separation. As dilatation advances, the placenta is separated and assumes new relations to the structures upon which it had been implanted. This being true, a complete presentation, when the internal os has been materially opened, will appear to be an incomplete or partial type; the marginal form will be evidenced as a partial or incomplete previa; and the lateral may have the placental periphery quite at the inter-

nal os. The placental rim which juts into the area of the undilated os has no clinical significance over the marginal form, so the word partial may with propriety be discarded.

These fundamental precepts lead us to believe that the following three types of previa cover every situation—lateral, marginal and complete—the type being visualized before effacement has taken place.

## FREQUENCY

Almost all pronouncements of the incidence rates of placenta previa (in fact, all obstetric phenomena) are based upon the experiences of individuals with special opportunities, or the numbers housed in their respective hospitals. Such figures are fallacious in that they do not reflect the prevalences of the anomalies in large aggregations of population. In the case of previa, the numbers which are coincident to abortions and miscarriage are never included as they are unavailable. Hospitals of necessity have a considerable preponderance of pathologic cases over other institutions which cater to a private clientele.

The Committee on Prenatal and Maternal Care of the White House Conference sent questionnaires to some 600 hospitals of the United States requesting a résumé of their obstetric statistics for 1929. No hospital was circularized which had not shown more than 100 births in a previous issue of the hospital number of the *Journal of the American Medical Association*. Of the 489 institutions which responded, 284 gave the numbers of previas attended by their physicians. These hospitals had obstetric capacities from 5 to 123 bassinets, and annual births from 97 to 3,228. In all, 1,024 cases of placenta previa occurred in this group. The average number of previas for each hospital was 3.9 cases. (Table 1.)

When we consider that a large proportion of our hospitals have almost as many obstetricians on the staff—let alone the numbers of "courtesy" members—as there are obstetric beds, we perceive the grave problem in giving physicians adequate training and adequate opportunities to develop experience. As nearly all computations of obstetric anomalies are based on hospital experience, they do not reflect true

TABLE I  
FREQUENCY OF PLACENTA PREVIA

Authority or No of Hospitals	No of Births	Total Births	No Placenta Previa	Average No per Hospital	Incidence	Ratio of Previa to Births
284*	97 to 3,228	151,857	1,024	3.6	0.67	1:148.3
45*	97 to 200	6,852	111	2.5	1.62	1:61.7
35*	1,001 to 3,228	51,399	276	7.9	0.54	1:186.2
1	97	97	4	4.0	4.12	1:24.3
1*	115	115	5	5.0	4.35	1:23.0
1	176	176	7	7.0	3.98	1:25.1
1	447	447	13	13.0	2.90	1:34.4
1	1,012	1,012	1	1.0	0.09	1:1,012.0
1*	1,313	1,313	1	1.0	0.08	1:1,313.0
1	2,174	1,214	1	1.0	0.05	1:2,174.0
D Findley		3,464,278§	21,706		0.63	1:159.6
Muller†		876,432	813		0.09	1:1,038.0
Schwarz‡		519,328	332		0.06	1:1,564.0

The enormous variations of incidence in different hospitals permit of but one deduction—the hospital statistics offer no clue as to the actual frequency in a large population—the only true basis for computation. Probably the actual ratio is between 1:500 or even 1:1,000.

\* From White House Questionnaire

† Mass statistics for the State of Oberhessen-Wurtemberg

‡ Mass Statistics for the State of Oberhessen

§ Estimated from data given

incidences. Until all lethal obstetric anomalies and their demises are nationally recorded we must accept a figure of not more than one placenta previa in 500 advanced pregnancies.

#### ETIOLOGY

**Contributory Causes.** It is quite generally believed that endometrial inflammatory alterations prior to pregnancy contribute directly or indirectly to the nidation of the ovum in the lower segment, but this belief is purely apocryphal. It is undoubtedly true that women who have borne children are more likely to have been exposed to infections as the result of opera-

tions, abortions or puerperiums than the woman in her first pregnancy. Multiparity is assumed to be a predisposing cause to the formation of a previa. Of eighteen previas in the Rotunda Maternity only one was in a primiparous woman. From the time of Rigby this has been noted; Smellie, Gifford and Rigby found that of fifty-one previas all but three were multiparae. Doran reported 316 previas with sixty-three present in primiparae—19.9 per cent. It is evident that multiparity does have some peculiar influence on the production of previa.

Age, too, has been given as an important predisposition to the formation of a previa. The value of the statement is somewhat negated in that one-third or one-fourth of all children are borne by women under 25. However, if endometritis, parity and age were potent contributory causes we would see frequent recurrences in the same woman. Yet a repetition of the complication is rare, and recurrence in three or more pregnancies is unique.

The writer is convinced that endometritis, multiparity and increasing years are interesting data for speculation, but are basically sequences of some unknown factor; he is strongly of the mind that future investigators will uncover a biologic reason for nature's selection of multigravidae for the ravages of previa. The influence of the endocrines upon every phase of reproduction—sterility, fecundity, development of the ovum, and changes in the endometrium—has been clearly proved. The aberrant influence is transitory, affecting the single nidation. Herein is a reasonable postulate for the contributory or even direct cause of placenta previa.

**Direct Causes.** Except for one explanation the putative direct causes are in the same realm as the contributory influences. Gravity was long held to be a cause, but whether the woman be erect, prone or supine the uterine axis is never long in the perpendicular, and its flexions militate against the theory. It is more tenable to believe that the ovum, bathed in the uterine secretions, is impelled downward by

ciliary motion and muscular activity. The decidual reaction may be delayed, so that only when the egg reaches the lower segment has the process been developed sufficiently for nidation. Possibly the fertilized ovum has not fully ripened and reaches maturity only when it comes in contact with the mucosa of the lower segment. As we know little of the physiologic reasons for implantation of the ovum above the retraction ring, we have no concrete explanation for its nesting below that area. It is an interesting actuality that a pure fundal attachment of the placenta is second in frequency to its location in the lower segment. Vascularity must bear an important part in paving the way for nidation.

**Reflexal Placenta.** Hofmeier and Kaltenbach (1888) offered a specific explanation for the production of a previa which was elicited by the study of decidual casts. They found early abortion specimens where the decidua reflexa had not yet coalesced to the vera. Cotyledons had sufficiently hypertrophied to be positively evident, some being attached to the vera while others were developing in the reflexa. The specimens clearly showed that the reflexal cotyledons were directed towards, and were near, the lower pole of the decidual cast. The accurate deduction was made that the reflexal cotyledons shortly would become adherent to the decidua vera in the lower segment, producing a previa.

Various authorities studied their specimens of decidual casts, and found repeated corroborative evidence of the truth of the assertions of Hofmeier and Kaltenbach. The growth of the reflexal placenta elucidates the method of the placenta's bridging the internal os. Noone has declared that this is the only method by which a placenta may develop as a previa, but others have maintained that it is but one method of production. Nearly all agree that the maturing placenta may reach and cross a tightly closed internal os without a reflexal origin.

A large placenta has been declared to be a cause of a previal placenta, especially as

the placental disc is quite commonly larger than normal. The large placentae of multiple pregnancies would clearly substantiate the allegation that large placentae are an element in that twins occur with twice the frequency in previa as they do normally. Some consider that the large thin placenta of previa is nature's endeavor to obtain adequate blood supply for the growing ovum. A placenta succenturiata may be present with either the parent body or one of the accessory parts presenting.

#### SYMPTOMS

Placenta previa has but one symptom—hemorrhage. The bleeding usually occurs without pain or even discomfort. If pain is present, it is almost invariably extrinsic to the previa, except in those instances where the placenta barely dips into the lower segment, and the escaping blood is retained for a brief period. The first bleeding may occur at any moment after nidation has occurred, and the maturing cotyledons show the first appearance of the future placenta. Before the fourth month the gestational interruptions have the distinctive features of an abortion or miscarriage, whether the previa is the cause or merely coincident. These early ovular expulsions due to previa are rarely reported, owing to remissness in studying the specimens. The infrequent reports do not imply an immunity to placental separation in the first trimester. The relative paucity of cases reported between the fourth and seventh months suggest that this is period of quiescence. It is credible to hold that in these months the placenta is in full maturity and secure against separation, while after the second trimester the progressive senility of the placenta may contribute to the readiness of the uteroplacental union to be severed under adequate stimuli.

David Findley reported that in 4,416 previas, 3,763 (84.98 per cent) patients had the first hemorrhage after the thirty-first week. According to the report of the Children's Bureau on Maternal Mortality in Fifteen States, 408 deaths from previa

were reported, of which 288 were recorded when the first hemorrhage took place: before the thirteenth week, seven (2.4 per cent); from the thirteenth week to the twenty-fifth, inclusive, thirty-one (10.7 per cent); from the twenty-sixth week to the thirty-ninth, inclusive, 201 (69.1 per cent); in the fortieth week, forty-nine (17.0 per cent). About 10 per cent of previas have the first hemorrhage when labor takes place.

The first hemorrhage was slight in 14 per cent, moderate in 26 per cent, and profuse in 60 per cent.

Bleeding may come on spontaneously, as the direct result of painless contractions, or because of the changing relations of the placenta at the beginning of retraction of the lower segment. It may appear during sleep, or in a quiescent period of wakefulness: the hemorrhage may be precipitated by coitus, may follow a local examination, or may result from blows, falls, or from other casualties, large or small. The amount of blood loss may be in direct proportion to the placental separation, or a large sinus may be exposed from a minimal disruption, resulting in an alarming hemorrhage.

#### DIAGNOSIS

Recognition of a previa may be obtained only by physical examination. Abnormal positions and presentations may cause a deviation of contour of the uterus and abdomen; their presence is corroborated by palpation. Abnormal fetal lies result from the presence of the placenta at the pelvic brim, which compels the head to take an eccentric position, and thus the development of transverse and breech presentations is favored. While these deviations of fetal position are common in previa, any pathology which disturbs the contour of the pelvic brim tends to produce the same effect. The deviations in position are presumptive evidences in the presence of bleeding during the last trimester, but prior to that time they are distinctly physiologic. Auscultation will corroborate the abnormality of position if marked, and will give indispensable knowledge of the

fetal condition if it is in jeopardy or is dead. If the placenta is situated anteriorly, auscultation may permit a detection of the bruit suprapubically. Müller reported that in 1,418 cases of previa, transverse presentations were found in 272 (23.8 per cent and breech in 107 (9.3 per cent).

Conclusive evidence of the presence of a previa may be derived from a vaginal or rectal examination, even before there is other suspicion of its existence. Routine local examinations between the fifth month and term would permit a diagnosis in all cases where there is a frank placental presentation, but the dangers of inducing a hemorrhage in the office from such examinations is ever present. The trite behest that a vaginal examination should be made at the time of the pregnant woman's first visit, and later only on some definite indication, has obtained these many years. However, one must determine whether it is preferable to give repeated, routine, local examinations as part of maternal care in order to isolate the rare woman with a previa, or to await the signal flare of hemorrhage before undertaking an examination. Which is the lesser of two evils?

The vaginal examination must be conducted under the strictest aseptic technique. Except under direct necessity it should be the rule that no vaginal examinations should be made unless all the paraphernalia requisite for immediate arrest of bleeding and all measures for terminating pregnancy are at hand. It is highly recommended to have the woman transported to the hospital, in an ambulance if one is available. On arrival she should be prepared for immediate delivery, the operating room set up for the emergency, and then only, under an anesthetic, should the parturient canal be entered. Exceptions to this dictum are few, for makeshift examinations are fraught with especial perils. Trained fingers elicit practically as much by rectal examinations as may be obtained through the vagina, and this does not carry risk of infection. Rou-

tine practice only is required to acquire proficiency.

The vaginal wall is commonly relaxed, and often cyanotic. The cervix is soft and relaxed, and usually the canal is dilated to some extent. In the area of the placental site there is an increased pulsation due to the undue vascularity of the tissues. In lateral and marginal types the cushion of placenta is found interposed between the finger and the presenting part, while on the opposite side the fetal part is more readily perceived. In a complete previa the fetus may not be felt at all, or only indefinitely.

It is usually possible to determine the existence of the previa without entering the cervical canal, but when this procedure is necessary it must be carried out with the utmost gentleness. The placenta alone is felt if there is a complete previa. If the placenta is marginal, the placental rim is easily palpated. In lateral forms the finger mounts a variable distance before the placental border is reached. The membranes, when palpable, are often thickened and the surface rough, due to the presence of thickened chorionic laeve and shreds of decidua where the sac has been stripped from its adhesions. The palpation of the placenta alone is proof positive.

*Roentgen Examinations.* Two methods have been suggested: (1) opaque dyes injected into the amniotic sac; (2) instillation of soluble dyes into the bladder. The former method is hardly worthy of consideration as the risks are too great, and, with our present knowledge, more accurate information may be obtained by more conservative methods. Cystography depends upon the fact that the placenta will raise the head above the normal station; to be suggestive there should be at least 1 cm. between the shadows of the opaque bladder and the fetal head. However, the contracted pelvis produces the same effect, or even a prolapsed ovary, kidney, etc., before the head.

Beck and Light made cystographic studies of 90 patients with vaginal bleeding. In the breech or transverse presentations

(nineteen cases) there was an error of over 20 per cent. In the seventy-one vertex positions there were eight errors and in seventeen true previas there were four conclusive results. Jablonski and Meisels believe the method is of value, though if there is a posterior location of the placenta it may be overlooked. Robecchi and Zocchi are of the opinion that the method is only of value after the seventh month; before that time the immature ossification of the fetal skull and its high station preclude all positive information. They further believe that there may be no differentiation of a previa from a severe ablatio placentae.

Under the circumstances these procedures should not be recommended for general use. Further progress in the hands of expert roentgenologists and obstetricians should be made before we may accept the methods as of any value. A timely vaginal or rectal examination will give conclusive information.

#### DIFFERENTIAL DIAGNOSIS

This phase of the subject will be discussed in the section on ablatio.

#### CLINICAL COURSE

The hemorrhages of placenta previa may manifest themselves at any period of gestation, from the earliest time until the onset of labor. The first hemorrhage is often slight, but may be profuse or fulminating. The bleeding may be a continuous dribble, or a protracted interval may elapse before the next bleeding recurs. Some few lateral and marginal previas have the first bleeding only in labor, but rarely does a complete previa manifest itself so late. However, instances have been recorded where the placenta, entirely separated, was expelled before the fetus, with slight risk to the mother. The medical attendant never should countenance such an unusual course. Spontaneous labor may occur in certain minor placental presentations, and here success is dependent upon the prompt descent of breech or head which will compress the bleeding area.



## PROGNOSIS

*Maternal.* The outcome for the mother afflicted with a previa is influenced by numerous circumstances. Her physical condition contributes to success or failure. The degree of previal presentation is of vital import as the maternal risks increase in proportion to the type from the high lateral to the complete forms. The amount of blood lost is of marked significance and the speed with which it may be arrested is a paramount issue. Promptness in augmenting blood volume, and celerity in blood transfusion are vital. A sudden violent blood loss is more serious than the same amount slowly escaping.

Lack of respect for minor bleedings in a pregnant woman may spell disaster; procrastination in the presence of any vaginal bleeding is unpardonable. It is stated in the report of the Children's Bureau (publication #223) that of 236 women dying of previa who had had a warning hemorrhage, only eighteen had received prompt treatment.

He who employs polypragmatic policies will have the maximum of disaster, especially if he performs cesarean sections routinely. Disaster awaits the surgeon who attempts a cesarean after others have futilely attempted a vaginal delivery. The conditions pro and con in each case must be weighed, and that operation selected which will give the maximum of success. One must appreciate that heroic surgery is not suitable to all cases of placenta previa. The best method is that which requires the minimal operative detail. Manual dilatation of the cervix, version, and rapid extraction form a trio of reprehensible obstetric practices.

Hemorrhage has a reciprocal reaction with anemia: the former creates the latter and the latter perpetuates the former by producing uterine atony and lowering the coagulability of the blood. Anemia makes the patient peculiarly vulnerable to the ravages of sepsis. When a previal patient dies from sepsis, the infection need not necessarily have been introduced from

without; often it is autogenous, the result of activation of the vaginal flora. The prolonged retention of the bag or tampon, the repeated vaginal manipulations tend to activate the bacteria. The blood in the vagina offers an ideal culture medium and the body heat provides the appropriate temperature. The proximity of the placental site to the potentially active germs, the exposure of abrasions to the purulence of the lochia all contribute to an autogenous infection.

Read (1861) and Müller (1877) presented figures which demonstrated the dangers of sepsis. The former recorded 229 previal deaths, of which thirty-eight (16.5 per cent) resulted from sepsis. The latter stated that, of the 212 deaths in his series, fifty-four (25.4 per cent) followed sepsis. Irving (1936) showed that, of twenty-two previal deaths, four (18.1 per cent) were due to the same cause.

The emergency obstetric service of large institutions necessarily must admit their quota of possibly or actually infected women. A full 50 per cent of all previal deaths result from ante- or intrapartal hemorrhage; a quarter of the patients succumb from a continuation of the hemorrhage into the third stage; the final group of deaths results from sepsis or some concurrent disease.

Since accouchement forcé has been repudiated, the dangers of postpartum hemorrhage or hemorrhage from lacerations have been greatly curtailed. Asepsis and sane conservatism have reduced the gross maternal mortality by 60 or 70 per cent, but sepsis continues to hold the same ratio to hemorrhage as the cause of a lethal result as before the antiseptic era. Table II shows the comparative results in various periods since 1860. To obviate confusion, lateral, marginal and partial placenta previas have been combined under the caption of "incomplete." Table IV presents the mortalities as influenced by treatment.

*Fetal.* The life of the fetus in utero is precarious even when its maternal environment is ideal. From the time of conception

until birth the fetus wages a losing fight and the fortuities of early neonatal life carry a heavy toll even under normal or average computations. When previa exists

has rigid indices. Statistics indicate not better obstetrics, but that in later periods the time of fair viability has been advanced.

TABLE II

MATERNAL MORTALITY RATES IN PLACENTA PREVIA (COMPLETE AND INPCOMLETE\*) IN DIFFERENT PERIODS

Authority	Total Cases				Complete			Incomplete*		
	Num-ber	Died	Per Cent	Per Cent Septic Deaths	Num-ber	Died	Per Cent	Num-ber	Died	Per Cent
Read† (1861).....	1,024	229	22.2	16.5	347	99	28.5	225	36	16.0
Müller† (1877).....	953	237	24.8	25.4	345	109	31.6	394	57	14.5
Holmes† (1905).....	2,756	213	7.4	....	350	47	13.4	1,022	44	4.3
Holmes† 10 reports from above.....	1,011	31	3.1	....	134	8	6.0	437	11	2.5
Holmes (1929) 256 Hospitals†.....	1,005	86	8.6	....						
D. Findley (1937).....	7,425	426	5.7	....	2,063	220	10.7	5,362	206	3.8
Irving (1937).....	308	22	7.1	18.3	77	11	14.3	231	11	4.8

Modified from Davis' "Gynecology and Obstetrics."

\* "Incomplete" includes lateral, marginal, partial.

† Cesarean sections not reported in these groups.

‡ Data derived from questionnaire of the White House Conference.

TABLE III

FETAL MORTALITY RATES IN PLACENTA PREVIA (COMPLETE AND INCOMPLETE\*) IN DIFFERENT PERIODS†

Authority	Total Cases			Complete			Incomplete*		
	Num-ber	Died	Per Cent	Num-ber	Died	Per Cent	Num-ber	Died	Per Cent
Read§ (1861).....	1,031	526	51.0	302	197	64.9	207	122	58.9
Müller§.....	2,365	1,518	64.2	320	223	69.6	382	182	47.6
Holmes§ (1905).....	1,985	1,075	54.1	216	174	80.5	538	272	50.6
Holmes§ (9 reports from above).....	381	147	38.9						
Holmes (1929) 158 Hospitals†.....	636	246	38.7						
D. Findley (1937).....	7,402	2,412	32.6	2,040	806	39.5	5,362	1,606	29.9

\* Incomplete includes lateral, marginal, partial.

† Modified from Davis' "Gynecology and Obstetrics."

‡ Data derived from questionnaire of the White House Conference.

§ Cesarean sections not reported in these groups.

every phase of fetal life is rendered tenfold more hazardous. The first hazard arises from the prematurity of the interruption of pregnancy. Unfortunately there is no generally accepted standard as to what constitutes prematurity; comparative statistics will be valuable when prematurity

Read (1860) and Müller (1877) considered that pregnancy was interrupted by placenta previa in 65.6 and 55.3 per cent respectively, their criterion of prematurity being after the twenty-eighth or thirtieth weeks. D. Findley (1937) found that 15.02 per cent of the pregnancies were terminated

prior to the thirty-first week; i.e., in 4,416 previas, 663 babies were born before that period. Irving (1937), at the Boston Lying-in Hospital, reports that of the 315 infants 116 (37 per cent) were born before the thirty-fifth week. Of the 315 babies, seventy-one (24.9 per cent) weighed less than 4 pounds. The fetus is also destroyed by the placental separation in pregnancy or labor. Irving states that forty-eight (15.2 per cent) were dead when the mother was admitted.

to mother and fetus it should ever be kept in mind. Cesarean section relieves the fetus of the stresses of birth, and the fetal results vie with those following spontaneous birth, with or without an artificial rupture of the membranes. The neonatal existence is beset with peculiar hazards since prematurity and impaired condition following birth render the infant particularly vulnerable to the maladies of the newborn.

Kuhn had forty-three previas in private practice—at the end of two months only

TABLE IV  
MORTALITY OF PLACENTA PREVIA AS INFLUENCED BY THERAPEUSIS\*

Therapeutic Methods	Maternal Mortality				Fetal Mortality		
	Number	Died	Per Cent	Per Cent Morbidity	Number	Died	Per Cent
Ruptured membrane†	2,070	37	1 8	4 8	1,958	436	22 2
Spontaneous birth†	3,068	70	2 3	4 8	2,244	525	23 4
Hydrostatic dilators	4,464	263	5 9	16 2	3,113	1,542	49 5
Hicks' version	10,660	686	6 4	23 2	8,213	5,523	67 2
Cesarean section	5,166	337	6 5	40 3	2,154	533	24 7
Vaginal tamponade	477	32	6 7		475	239	50 3
Accouchement forcé	291	71	24 4	22 6	282	133	47 2
Totals	26,196	1,496	5 7	..	18,439	8,931	48 4
Findley's grand total	47,828	3,454	7 2	.	27,047	14,427	53 4

\* Adapted from Findley's analysis of 47,828 cases, with relative morbidity rates as reported by Irving. Modified from Davis' "Gynecology and Obstetrics."

† Dr. Irving rightly considers these two together as expectant treatment.

The causes of death in previa are (1) asphyxiation (directly due to placental separation or due to the placental compression in birth, cutting off aeration of the blood), and (2) hemorrhage from the lacerated placental tissues. Blood counts on live infants and on dead ones born before coagulation has set in will clarify this postulate. If fetal death is due to acute anemia, a timely blood transfusion might save some.

Finally, the type of intervention has an enormous influence on the life expectancy of the fetus, just as is the case with the mother. The simpler the intervention the lower the gross fetal mortality; the more drastic the operation, the greater will be the fetal loss. As this dictum applies equally

two infants remained alive. It is an interesting sidelight that in the 47,828 previas collected by Findley the status of the baby after birth was mentioned in only 27,074 (56 per cent). That no mention of the outcome of the fetus was given in 44 per cent illustrates the scant regard too many reporters grant the fruit of the pregnancy. The fetal mortality rates are presented in Tables III and IV.

#### TREATMENT

*General Considerations.* Two imperative demands exist in the therapy of placenta previa: the first is that bleeding shall be arrested at the earliest possible moment, and that there shall not be recurrences; the second that measures shall be taken which

will eventuate in the termination of labor. The first is accomplished by two expedients which are the precursors of the second, the tampon (ordinarily an abomination) and the hystereurynter serve this purpose. Hicks' version is valuable in both spheres. The great advantage in these three is that during the period of waiting active measures may be taken to combat the ills of the anemia, and to provide supportive treatment.

cesarean section who are tainted with a possible infection, who are in a distressing condition from shock and hemorrhage, or, ordinarily, whose fetus is dead or in such a precarious state that there is no reasonable expectation it will survive the ordeal of the operation. Such circumstances belie the putative advantages of section, and in these cases another type of delivery is chosen to absorb the evils and dire consequences.

TABLE V

COMPARATIVE FREQUENCY OF ABLATIO PLACENTAE AND PLACENTA PREVIA FROM THE SAME SOURCES

Authority	No. of Births	Ablatio Placentae			Placenta Previa		
		No.	Incidence	Percentage	No.	Incidence	Percentage
Churchill	68,982	85	1:811	0.12	171	1:403	0.25
Smyly	61,453	70	1:877	0.11	41	1:1499	0.06
Irving*	34,392	353	1:97	1.03			
Irving*	28,391				308	1:111	1.08
Solomons	2,376	29	1:82	1.22	18	1:132	0.75
N. Y. Lying-in Hospital, 1934	2,637	9	1:293	0.34	13	1:203	0.49
N. Y. Lying-in Hospital, 1937	2,732	13	1:201	0.45	15	1:182	0.55
N. Y. Lying-in Hospital, 1938	2,923	8	1:365	0.27	19	1:154	0.65
Chicago Lying-in Hospital, 1925-1927	6,097	48	1:127	0.78	48	1:127	0.78
Holmes, 123 Hospitals W. H. C., 1929	100,016	555	1:180	0.55			
Holmes, 284 Hospitals	151,857				1,024	1:148	0.67
Totals { Ablatio	281,608	1,170	1:241	0.42			
{ Previa	327,448				1,657	1:197	0.51

\* If the incidence and the rate for ablatio were calculated upon the combined births of the "In and Out Services"—60,334—the incidence and the rate would be reduced to 0.57 per cent, i.e., 1:170, and 0.59 respectively. On the same basis the hypothetical incidence of previa would be 1:194, and the percentage would be 0.61. As the computations for the two hemorrhages are based upon hospital experiences they do not reflect the frequencies in the community as a whole; 1:500 for each would be a conservative conjecture.

No single procedure fulfills every purpose. One must weigh the evidence and employ the method which is indicated, and must elicit the conditions which will determine the appropriate course. The highly trained expert, in an ideal environment, may adopt methods which are not permissible for the attendant who may have occasion to treat a previa once or twice in a lifetime. The reader must scrutinize Table IV with a judicial mind, for the results obtained by the different therapies are not quite what they appear. For example, the circumspect will not select women for

*Blood Transfusions.* The replacement of lost blood when of material amount is imperatively required, for transfusions not only renew the blood volume but stabilize its quality, and greatly reduce the possibility of shock. They are so important that every institution which receives patients with puerperal hemorrhages should have facilities for their administration. The availability of donors and the possession of all the equipment for this purpose is no great problem in a large service, although in a small institution there are difficulties which must be met. These may be over-

come if a group of regional community hospitals coöperate to form a "blood bank" in the most centrally located hospital. Irrespective of the amount of blood loss, all hemorrhage patients admitted should routinely have a blood typing, blood count, and hemoglobin estimation. At the moment they may not be required but the timely investigation is more desirable than a

section is performed, on indication, the instillation of a half to a full liter of decinormal solution into the abdominal cavity is invaluable, as suggested by Howard Kelly.

Of the various recourses in the treatment of previa, some are highly lauded, others condemned. The measures are: (1) temporizing; (2) awaiting spontaneous birth

TABLE VI  
FREQUENCY RATES AND GROSS MATERNAL AND FETAL DEATH RATES IN ABLATIO PLACENTAE\*

Authority	Total Deliveries	No. of Ablatios	Percentage	No. of Ablatios	No. of Maternal Deaths	Percentage	No. of Ablatios	No. of Fetal Deaths	Percentage
Goodell† (1870)	.	.	.	106	54	50.9	106	100	94.4
Holmes† (1901)	.	.	.	189	61	32.2	184	158	85.8
Willson† (1922)	.	.	.	69	31	44.9	67	62	92.5
Holmes (1922) personal cases	.....	.....	.....	22	2	9.1	22	13	60.9
Cragin (1916)	20,000	212	1.06	212	12	5.7	212	122	57.5
Harrar (1917)	100,000	254	0.25	254	22	8.7	254	158	62.2
Burgess (1925)	18,720	80	0.43	80	6	7.5			
Fitzgibbon (1926)	55,000	115	0.20	115	11	9.5			
Brodhead (1927)	16,500	34	0.20	34	9	26.4	34	29	85.3
Kraul (1927)	15,000	27	0.18	27	2	7.4	27	17	62.9
Goethels (1928)	12,032	128	1.06	128	11	8.6	128	79	61.5
Wing (1928)	60,000	164	0.27						
Bartholomew (1929)	9,208	61	0.66	61	4	6.5	61	51	83.5
Williams	9,000	57	0.63	57	4	7.5	57	41	72.5
Davis-McGee (1931)	40,000	164	0.41	164	12	7.3	164	98	59.7
Irving (1937)	60,334	353	0.59	353	18	5.1	357	170	47.6
Bland-Rakoff	.	.	.	2,319	146	6.3	2,319	1,539	66.4
Totals	415,794	1,640	0.39	3,962	290	7.3	3,702	2,379	64.3

\* After Davis and McGee, Irving, and the literature.

† The mortality data of Goodell and Holmes were not included in casting the total mortality rates, as the cases were treated from the early eighteenth century to 1900. They are given to contrast the old and modern mortality rates.

‡ Willson's sixty-nine cases were proved examples of Couvelair's uteroplacental apoplexy.

hurried examination when an emergency arises. Where neither paid donors nor blood banks are available, a call should be made upon members of the family to come to the hospital for a grouping; then, the selected donor should stand by until it is clearly evident the blood will not be required. If blood is not available an opportune saline transfusion will raise the blood volume. According to the exigency of the case the saline should be given intravenously, subcutaneously, or rectally. If a cesarean

with such minimal ministrations as rupture of the membranes; (3) vaginal tamponade; (4) hystereuryesis, either awaiting subsequent spontaneous labor, or more commonly, the internal version; (5) Hicks' version; (6) Willett's forceps, either as the sole expedient, or as an adjunct to other methods; (7) cesarean section; (8) accouchement forcé, including Dührssen's incisions and vaginal cesarean section; (9) management of the third stage.

*Temporizing.* Placenta previa is a malignant affliction which demands prompt eradication. From the moment the physician becomes master of the field he should not retire until the patient is safely delivered or dead. Procrastination is disastrous. If an exception does exist it should be limited to the elderly primigravida, or childless parous woman, where a future pregnancy may no longer be a possibility. The physician should raise every objection to a delay, should positively explain to the patient and family the foolhardiness of such a course. It is a wise precaution to have his behests in writing, and a documentary evidence from them that the patient's imperious demands for the safety of the child outweighed any anxiety for herself. The patient must be hospitalized during the entire period of waiting and she must never be left alone. Written instructions should be in the possession of nurses and interns so that immediate action may be taken if bleeding recurs. A second hemorrhage should brook no delay.

*Spontaneous Labor—Rupture of the Membranes.* Singly or in combination, these methods are especially applicable to lateral and marginal previas and they may also be considered where a placental portion, torn away, is pendant in the birth canal. The prerequisite condition are: (1) the fetus must have a cephalic or breech presentation; under no circumstance should a shoulder present; (2) there must be no impediment to delivery; (3) hemorrhage must not be profuse. It is very desirable that there shall be uterine irritability, or, better, a definite onset of labor. The vulvar field should be surgically prepared for delivery, the membranes ruptured, and the liquor amnii be permitted to drain away slowly. It is well to keep the fingers in the vagina while the fluids are escaping so that one may determine that the fetal pole is descending. This process will permit the fetus to compress the bleeding surface. Watchfulness is imperative. If spontaneous delivery does not eventuate, then, when the presenting part is deeply in the pelvis,

either a low forceps or modified manual aid should be carried out, as indicated. The extraction must be performed slowly, never hurriedly. This is the safest procedure for mother and baby as it obviates a major operation.

*Tamponade.* The use of the vaginal tampon is to be deprecated. It is rarely used by the specialist, but for the man of limited experience it is a very safe method. If the woman has had a dangerously severe hemorrhage, even a slight one, and must be transported to the hospital, it hardly seems justifiable to avoid its use. The memory of a physician who was called to a patient under allied circumstances is ever fresh. He felt it his duty to get the patient to the hospital promptly; the moment the woman was in the ambulance he rushed ahead to get the operating room prepared, but when the patient arrived at the admission door she was dead from hemorrhage.

The technique of applying the tampon is of extreme importance. The vulva must be thoroughly prepared. If the bleeding permits, the vagina may be swabbed out with mercurochrome or other approved antiseptic. Strips of gauze are inadequate. Sterile absorbent cotton must be used. The pledgets of cotton (the size of hickory nuts) are soaked in an approved antiseptic solution, as liquor cresolis or mercurochrome. The antiseptic is necessary so that putrefaction may be minimized. A large speculum is introduced and held in place by two fingers of the left hand in the vagina. The right hand passes the pledgets into the vagina, and the left fingers build up a firm ring about the cervix. Whenever a depression is found, a piece of cotton is crowded into it. The tampon must be tightly applied, as otherwise it is useless. When the packing has been completed, a large vulvar pad is applied and is held in place by means of a T binder. Under no circumstance should the tampon be left in place longer than twelve hours. The tampon is removed in the operating room, with a complete set-up provided. One may do one of three things when the tampon is removed,

depending on the condition of the cervical canal: (1) a hydrostatic bag may be placed; (2) a Hicks' version performed; or if these are impossible, (3) then one may repack until labor has progressed sufficiently to suggest that dilatation has occurred, when an internal version may be done. While repacking is strongly inadvisable it may be the best course if the attendant be inexperienced.

*Hystereuryesis.* The bag is invaluable in a clinic where there is a frequent call for it, and where replacements are readily obtained. In small community hospitals where the bag may not be used over periods of many months, the rubber and the fabric may so deteriorate that bags are out of the question. Another objection is that once the bag is in place, the whole operating room force must remain for immediate action if the bag is expelled. If the cervix is soft and relaxed, the bag may be extruded in a very few minutes, while if it is firm and labor is not induced, many hours may elapse before it is forced out. The writer was once called to a small hospital where a bag had been employed for a previa. The operating room force went about their various pursuits, leaving the patient to a nurse to watch. The bag came away unexpectedly and before the staff could be reassembled the patient was exsanguinated, and she died shortly.

After the bag is in place and the stem ligated (never using an artery forceps for the purpose)—a 2 pound weight is attached to a cord extending to a few inches from the floor. It is a wise expedient to ligate the stem at the vulva that there may be a marker to denote the descent of the bag as dilatation progresses. If progress is not made within twelve, or at the longest, eighteen hours, the bag should be removed, and a fresh one inserted, unless sufficient dilatation is present to permit Hicks' version. In some instances the os is so closed that a version may not be done, so that a bag is employed to secure enough opening for the Hicks' maneuver.

The bag is invaluable in marginal, the so-called partial, and even for central types. It should invariably be inserted intra-ovularly. When placed within the sac it compresses both the placenta and its site, and has the advantage that since it rests on membrane which will eventually be expelled. If placed extra-ovularly it efficiently controls the placental site, but does not do so to the placenta, and may cause additional placental separation: the dangers of sepsis are more acute as the bag rests directly on the denuded site. In incomplete forms it merely is necessary to rupture the membranes before insertion. In complete cases, if an edge may not be palpated, the placenta is perforated and the bag passed through the rent. In every case the bag must be distended with a sterile fluid. If the bag is used as a preliminary measure before a Hicks' version, or if later an internal version is accomplished, the fetus invariably must be left for spontaneous expulsion—under no circumstance should there be rapid extraction.

*Hicks' Version.* During the near 60 years since Braxton Hicks devised the combined external and internal version which bears his name it has stood the test of time. It is conceded to be the best method, especially if the fetus is dead, for those whose training makes them an adept in the technique. There is no question but that the fetus may be turned with consummate ease if there is ample liquor amnii, yet many times the task is so difficult (as in oligohydramnios) that it tries the most expert. The bleeding which may accompany the procedure is disconcerting to an untrained man.

The os must be dilated sufficiently to admit two fingers, the vagina sufficiently relaxed to admit the hand, the membranes intact, or so recently ruptured that no retraction has taken place. The ideal is so to manipulate that the membranes are not ruptured until about the time the leg is to be brought down. The operation is contraindicated in the presence of actual cervical rigidity, but the cervix unprepared for

dilatation may be relaxed by means of preliminary use of the rubber bag. A cervix unprepared for delivery is not to be considered one of rigidity. Cervical rigidity has been often certified to have warranted a cesarean section. However, personal communications from seven authorities (in 1905) with a total of 626 previas stated that the authors never had seen a true rigid cervix associated with previa.

The great advantage of Hicks' version lies in the fact that the smallest part of the fetus (the breech) passes through the cervix first, and the largest part, the head, last, so that the bleeding area is constantly being compressed.

*Willett's Forceps.* These forceps are a modified volsellum whose purpose is to permit traction on the head. They grasp the fetal scalp, and are applied whether the infant is alive or dead. It is alleged that they are harmless, but as the fetal mortality with their use is fairly high it is presumptive evidence that they do offer risks to the baby. The forceps must take a sufficient bite of the scalp or else they may pull off, thereby lacerating the tissues. It is claimed that they are applicable before a Hicks' version may be done, as only one finger dilatation is prerequisite, but as they must be applied blindly it is difficult to believe that they may always be effectively clamped to the head.

F. J. Browne found that this instrument was used 252 times, with a maternal mortality of 3.5 per cent and a fetal mortality of 46.4 per cent in a series of 3,103 previas treated in eleven teaching hospitals. He protests against their use, as asphyxia is produced since the head compresses not only the maternal placental circulation but that of the fetus as well. These allegations are spurious since this is the desirable effect in the use of the bag and the breech expulsion after any type of version. The compression of the bleeding surfaces by the fetal body is the ideal way of arresting hemorrhage.

When the forceps are applied a weight of not more than 2 pounds is applied in the

same manner as for the hystereurynter. These forceps should not be considered a means of dragging the fetus through the canal, but merely for the purpose of keeping the fetal head in close juxtaposition to the bleeding surfaces. The advantage of having the largest part of the fetal body coming through last (in breech) is more than a theoretic one. The use of these forceps is worthy of further consideration and trial, as it obviates definite risks incident to version.

*Cesarean Section.* The first cesarean section deliberately done for placenta previa was probably performed by Sligh (1892). He resorted to tamponades for over a day, used hydrostatic dilators, ruptured the membranes, and what else(!), and then turned to cesarean section as a last resort. Mother and baby died. Between that time and 1905 some twenty-eight additional operations were reported. Inspired by Lawson Tait who stated he had no experience with obstetrics, and Deaver who knew surgery but did not know obstetric surgery, cesarean section became the resort of surgeons and general practitioners long before obstetricians had a chance to clarify the atmosphere by designating the principles which should guide clinicians in the selection of cases suitable for the operation. Before their preachments prevailed, sections were performed without regard to the mismanagements which preceded the interventions. Yet, as late as 1935 (Children's Bureau, Publication #223) forty-one previal deaths preceded by sections had prior tamponades, and others gave suspicion that operative attempts had been made from below. Truesdale (1903) issued this dictum: "*Cesarean section should be done before anything else has been tried, or not at all.*" Obstetricians have repeatedly iterated this behest, but with little avail. Cesarean section for placenta previa is the strongest arm we possess, in appropriate cases, and about the worst if there have been antecedent attempts at vaginal delivery.

Definite conditions should obtain to justify the procedure:



1. There should be a freedom from potential or actual sepsis.

2. The section should be the primary operation (tampons or bags shall not have been used, or other manipulations tried). A diagnosis of previa cannot be made without a vaginal examination; this should be done with the most meticulous regard to asepsis.

3. The woman should be in good condition with minimal anemia, for anemia begets shock and a vulnerability to sepsis which are the great contributors to the death toll. A timely blood transfusion combats these evils. At best puerperal morbidity is approximately twice as frequent as after all other methods of delivery.

4. The fetus should be alive, in good condition and not be a teras (as proved by x-ray), and the pregnancy should have advanced beyond the period of prematurity.

5. The previa should be complete.

6. Abnormalities of the parturient canal offer strong contributory indications, such as contracted pelves or marked pathologic changes of the soft parts.

There is no question but that deviations from these strict admonishments may occasionally be demanded. When available, the expert obstetrician should be called to sum up the indications and the contraindications. At times, his acumen will be sorely taxed. Obstetric problems are inherent to the specialty. Good surgical principles do not always coincide with sound obstetric tenets.

It is advisable that a supravaginal hysterectomy follow the section if there is sepsis or if the patient has been exposed to vaginal manipulations. This operation was first suggested on theoretic grounds by Blundell (1834), but it is to the credit of Horatio R. Storer that he performed the first operation on a puerperal woman some ten years before Porro published his paper. This essential step must ever be kept in mind by those who manage a previa by cesarean section, as a precaution against a septic death. It may also be required if there is excessive uterine atony.

Whatever merits lower segment cesarean section may possess over the classic procedure for diverse indications, it still remains a moot question in placenta previa. In the years past many sites for the classic incision other than the anterior midline were elected to obviate the putative risks of a placenta previa cesarean. Some of the arguments against having the incision in the placental site were valid, others were rather illogical. We agree with Irving that there are definite objections to the low section for previa and that the management of the third stage may be controlled better through the classic cut. There may be, and often are, gross textural changes in the lower segment and cervix incident to the abnormal implantation. This, coupled with the risk of miscalculating the length of the incision in cervical cesarean section, may cause a deep tear into the portio vaginalis. The common necessity of readjusting the position of the head and application of forceps may cause additional placental separation and hemorrhage—and certainly delays the extraction of the fetus. In addition, the classic operation may be more quickly performed than the low section, and is better for the casual operator.

The average maternal mortality of cesarean section for placenta previa is 6 to 7 per cent, as given by various statisticians; in special clinics the rate is lower. The fetal death rate is 55 to 60 per cent, though Irving reports a gross fetal loss of 23 per cent.

Contracted pelves offer the great typical indication, if the mother and child are in perfect condition, where there may be a minimal loss of life. Anesthesia and some rare contingency may determine death. The operative risks are invariably present, but when the indications per se indicate high maternal and fetal dangers the operation carries a dual load. Cesarean section is neither a simple nor a perfectly safe operation. In 1929, 335 hospitals reported to the White House Conference 4,889 cesarean sections with 292 deaths, or 5.97 per cent. Of these, 161 hospitals reported 1,625

sections without a maternal death. Therefore, the remaining 174 institutions had 3,264 operations, among which were 292 deaths—8.9 per cent. Of these 174 hospitals, ninety-seven (55 per cent) with 776 operations had a death rate of 20.7 per cent. In fifty-three hospitals the rate was 32.2 per cent; in thirty-three it was 44.2 per cent; in eighteen it was 60.5 per cent; and in seven, with eight operations, it was 100 per cent. In 190 reporting hospitals the fetal death rate was 8.79 per cent; sixty-four hospitals with 413 operations lost no infants. The hospitals with reported deaths had a rate of 10.0 per cent; seventy-eight hospitals lost over 10 per cent of the infants; thirty-five lost over 20 per cent; twenty-two, over 30 per cent; eleven over 40 per cent, and in five, the ten babies died in ten operations.

How much the average death rate has been lowered these ten years may be proved by a comparable comprehensive study. Placenta previa is a fortuitous circumstance, not to recur. During the rest of the woman's reproductive life hovers the menace that if she conceives again and attempts a spontaneous labor a rupture of the uterine scar may occur with its calamitous result to her and her baby. At best, in each pregnancy she requires a terminal section to evade the accident.

The postoperative course, at the very best, is fraught with a potential morbidity. At least half of all patients with cesareans for placenta previa run some febrile reaction indicative of a degree of infection which jeopardizes the integrity of the scar. The writer has always taught that puerperal "morbidity" was a euphemism to gloss a low grade infection. The old axiom, "once a cesarean, always a cesarean" cannot be disregarded.

Conditions being as they are, we feel that cesarean section is not to be recommended as the happy means of treating placenta previa, though in some instances it is the only wise course. Promiscuity in its use cannot be condoned. One of the vaginal methods of management should be elected

by the general practitioner. If the abdominal route is deemed the logical means of termination of the case he should select the best available abdominal surgeon to relieve him of the responsibility. *Make the section the primary operation—do not select the procedure as a wise solution after futile vaginal endeavors have accomplished nothing.*

*Accouchement Forcé, Dührssen's Incisions, Vaginal Cesarean Section.* These methods are grouped under one caption as objections to them are in a common category, and their effects on mother and child are unreasonably and dangerously high. The worst era in obstetric history was that period when brusque, even violent, measures were employed to accomplish a quick delivery. Manual dilatation, or the use of the Bossi type of instrumental dilatation, upon a friable cervix merely brought an unconscionably high mortality. Then to drag the fetus rapidly through a partly dilated or illy prepared tissue was but to complete what the artificial and rapid dehiscence failed to accomplish—a tearing high into the lower segment or into the parametrial structures. In those days, one-half the deaths resulted from the previal hemorrhage itself, one-quarter from bleeding from cervical lacerations, and the final quota from postpartum hemorrhage. Condemnation of this method is obvious.

Dührssen's incision and vaginal cesarean section are allied in that both must often be performed in a pool of blood which may interfere with the identification of the tissues and the determination of the extent of the incisions. They both necessitate immediate extraction of the fetus. Essen-Möller, after an experience with twenty-seven vaginal sections, severely condemned the procedure, and stated that one may never gauge the proper length of the incision nor the extent of tearing which will ensue when the fetus is pulled through the opening.

#### THE THIRD STAGE

The dangers of previa are not over for the mother with the birth of the baby.

From the nature of a placental presentation, implanted upon the lower segment with its minimal retractility, aberrancies in the course of the third stage are frequent, though not necessarily constant. The more completely the placenta is located within the lower segment the greater is the likelihood of deviation from a normal course; per contra, the higher the lateral previa, the less the interference with the normal course of placental expulsion. Endometritis and deciduitis are not infrequently present and these are conducive to placental adherence. The lowered retractility and the general uterine atony induced by anemia are also factors. Further, the placenta is often lacerated to a high degree, and to the unwary may be the cause of a retention of placental remnants. Among them, these difficulties may produce a postpartum hemorrhage and cause the death of a woman already exsanguinated from ante- and intrapartal bleedings.

In the absence of bleeding, the following measures should be taken: The vulvar area is cleansed anew. A tape encircles the funis at the vulva to serve as a marker for the descent of the placenta. A large pad is placed over the vulva and the hand lightly controls the uterine fundus (noting contractility and retractility). The vulvar area is constantly kept under observation for undue bleeding, while the pulse and facies are frequently noted. When the placenta has left the uterus, as determined by the size, contour and the advancement of the cord, an Ahlfeld expression is practiced. At times the placenta will be spontaneously extruded. An ampule of pituitrin may be given immediately after the fetus has been born; this is especially indicated if there is any bleeding of consequence. Ergot and a second dose of pituitrin are indicated after the placental stage.

If there is any amount of bleeding in the third stage a Credé should be employed after message has secured a contraction, and not before. If bleeding is profuse, and massage and Credé fail to empty the uterus, a manual removal of the placenta

should be carried out. Care must be taken that the placenta is removed intact; if tearing does occur there must be certainty that all placental fragments are removed. Every fragment should be kept, and an attempt made to rebuild the placenta into its original form so that one may be certain of total removal. If bleeding persists from atony or from lacerated cervical surfaces, a snug uterovaginal tamponade should be employed. Gauze, sterile and antiseptic, only should be used. The gauze should be in *one piece*, one-half yard wide, folded into a "tape" with the frayed edge folded inward, and 10 yards long. Depending on the size of the uterus (whether in prematurity or at term) 5 to 10 yards of gauze will be needed. The writer devised a uterine packer for this purpose some forty years ago and can vouch for its efficacy and safety. With its use the gauze touches no living tissue from its exit from the container until it is in situ.

#### SUMMARY

The essence of therapy for placenta previa includes these measures:

1. Arrest hemorrhage promptly (respect blood losses) by Hicks version, or by hystereuryesis, or even by the objectionable tampon when needful.
2. Give timely *blood* or saline transfusions on indication.
3. Employ measures for delivery which are *slow* but sure.
4. Whatever the temptation may be, never practice rapid extraction of the fetus.
5. Circumspect management of the third stage.
6. On proper indication tampon the uterus and vagina—*never the vagina alone*.
7. Never repair the lacerated cervix unless the woman is in a remarkably fine condition. A secondary repair is always strongly desirable. If the tear bleeds the *uterovaginal tampon* will arrest it. A vaginal tampon is a transgression.
8. The routine swabbing of the vagina with an approved antiseptic (mercurochrome or liquor cresolis), where possible,

will sterilize the vagina to a degree: or these antiseptic may be instilled into the vagina by means of a catheter. Bichloride

of mercury is absolutely contraindicated where there is blood or its serum, as was pointed out by Lister himself.

## ABLATIO PLACENTAE

The separation of the normally situated placenta, or other designating terms credited to be synonymous, do not define specific entities, but are generic, covering a protean group which have two outstanding characteristics in common—placental separation and sequential hemorrhage. Our knowledge of the broad subject has sufficiently advanced to permit a segregation of the variants into four etiologic groups. The future will determine how much further this number may be extended as the specific causes are recognized. Then the symptom complex for each will probably be clearly appreciated, permitting a clinical diagnosis as the types present themselves. In fact, the toxemic forms may be so differentiated at the present time.

Since A. C. Baudelocque (1804) described and named a type of detachment where the entire blood loss was retained within the uterus, clinicians have recognized concealed and open hemorrhages. The difference is an interesting phenomenon, but every sign and symptom which occurs in the one is equally prominent in the other. Overt bleeding must never be taken as the diagnostic sign, but should be considered merely a corroboratory evidence. The diagnosis must be based on the facts, and should not await external bleeding. As the Mayos put it, liver disease should be diagnosed before jaundice appears, not after. Complete retention of the blood is merely the result of mechanical processes; in the course of moments or hours the mechanical obstructions break down and some blood escapes. When bleeding becomes patent the amount which escapes is never commensurate to the amount lost to the circulation (stored within the uterus). In order to clarify the nomenclature the writer has taught that the bleeding is *absolutely* or *relatively concealed*. Other writers differentiate be-

tween incomplete and complete placental separation.

### FREQUENCY

Several postulates must be conceded before we may derive an intelligent computation of incidence. First, there must be a division into cases of pathologic interest and of clinical significance. The pathologic type is fairly common: routine examination of placentae reveals that the maternal surface contains one or many small, old clots, indicative of a pathologic alteration of the organ with capillary hemorrhages. These will be found in one placenta in 100, or one in 200 inspections. They must be not confused with flocculi or minute masses from Schultze's retroplacental clots. From the clinical viewpoint these hemorrhages must be segregated from the cases of clinical import. Harrar (1917) stated the matter tersely in discussing the incidence rates, "we only included those cases which were of sufficient moment to permit a diagnosis, or required treatment." On this basis he cited that all types of ablatio occurred once in 170 deliveries in the ward service, and once in 1,085 births in the outpatient department. The latter figure probably reflects the incidence in the community as a whole.

As has been stated, both placentae previa and ablatio placentae in a technical sense may occur any moment after the chorionic cotyledons begin to assume the characteristics of a rudimentary placenta. Retroplacental hemorrhages are almost constant accompaniments of placental separations in late abortions, including the period of immature development of the ovum, and are comparable to the retrodecidual hemorrhages of the very early abortion. Cognizance of this is never taken in any estimation of premature separations; the hemorrhages are reputed

to be peculiar to the early interruptions of pregnancy.

#### ETIOLOGY

The alleged etiologic influences for the production of a premature detachment vie with eclampsia in the multiplicity of theories.

*Predisposing Causes.* Parity has been considered without ample proof as a contributory factor, but it is of small moment. Of the writer's 200 cases the parity was given in 156 and 19.2 per cent were in primiparae. Brodhead reported 21 per cent, Davis and Colvin 36.6 per cent in this group.

Age is of negligible influence. The placenta is the one structure of the human body (ignoring that it is a part of a parasite) which is physiologically extruded when it has fulfilled its mission; the line of cleavage is definitely present in the decidual stage, and persists until the senile placenta is shed. Mesnard (1753) fully amplified this anatomic fact and Jacquemier (1887) substantiated it, explaining that the enormous ramification of fetal and maternal vessels, with a delicate barrier between, offers an inviting field for apoplexy and placental separation. When their structure is altered by inflammatory reactions or degenerative changes their integrity is doubly jeopardized, only requiring an abetting influence to precipitate a severance of the union.

*Direct Causes.* Knowledge of the etiology has sufficiently progressed to warrant the assumption that at least four groups of causes may be enumerated and it is not chimerical to believe the symptom complex for each will be segregated, and a clear clinical differentiation between them will be possible in the future:

1. Casualties and trauma.
2. Pathologies—inflammatory or degenerative changes of the serotina.
3. Toxemias—possibly not one but several forms.
4. The uteroplacental apoplexy of Couvelaire.

*Casualties and Trauma.* It was natural for writers of the past to have sought diligently for a traumatic origin, sincerely thinking that "accidental" connoted this, and not recognizing the correct sense of its fortuity. One of the ablest writers recently perpetrated this error. Of the writer's 200 collected cases, sixty-seven (33 per cent) were considered due to this cause, though over a hundred years ago J. Ramsbotham pointed out that there was not an immediate correlation of cause and effect. Some of the present authorities would decry the importance of injuries; of all the viscera of the body the growing uterus is the only one which is unprotected and directly exposed to attacks. We cannot escape the effect of trauma, though our modern conception of cellular pathology relegates it to a lesser rôle. When trauma does occur it is tragic in effect.

Bartholomew and Colvin aver that fetal movements, and J. W. Williams that hypertension, will cause separations when directed to degenerated villi; severe blows, jars, falls, whether directly or by contrecoup, may likewise be effective. We have an analogy in rupture of the abdominal and thoracic viscera, though no one has maintained that this can occur only in a diseased organ. Intra-uterine manipulations, such as version or the induction of labor by catheters, have caused the disaster of an ablatio. Gendrin (quoted by Cazeaux and Tarnier) maintained that contractions alone were causative, and the contractions and retractions following the birth of the first of twins, or the precipitous evacuation of a polyhydramnic fluid have sometimes been responsible. The short cord may pull the placenta from its attachment; in the writer's collection six instances were recorded. We cannot deny that an outburst of emotions plays an important part. In the course of great public catastrophies many women will have severe hemorrhages and interruptions of pregnancy from this cause.

*Pathogenic: Local Inflammations and Degenerations.* An antecedent endometritis with a continuation during pregnancy

as a deciduitis has long been considered of importance in the production of premature separation. In such involvements it would be inevitable that the basalis would be affected. In the writer's series of cases reported before 1900, endometritis, deciduitis, scirrhus of the uterus, exudative myometritis, and "fatty degeneration of the decidua were mentioned."

Rokitansky described placentae which had inflammatory deposits in the lobules expressed in a thickening of the endothelium of the terminal circulatory vessels, even obliterations of the capillaries by thrombosis. Infarcts were often mentioned. Slow infarction is the characteristic of a large proportion of all senile placentae. As far back as Fehling (1887) infarctions played an important part in the discussions on the cause of ablatio. He and Schroeder (Ohlshausen and Veit-1899) asserted that we must go further before we may declare infarctions in women with nephritis different from those in normal placentae. This matter on which Bartholomew and Colvin have made many enlightening pronouncements, will be resumed in its appropriate place.

Fatty degeneration, present in senile afterbirths, has been stressed as a causative factor. Fibrosis of the placenta has been a putative element. Calcareous degeneration in the nonpregnant uterus is known to be accompanied by hemorrhages. Calcareous deposits in the placenta may hold an allied position. Though calcification is present in presumably normal placentae, it is logical to believe that this factor may be causative in the presence of a strong impulse, as is the case in cerebral apoplexy.

However, many placentae in traumatic or spontaneous ablatio show no morphologic changes other than the markings of a senile organ.

Syphilis has long been known to produce gross and microscopic alterations of the placental structure. Spirochetes have been isolated in the organ, yet this disease holds but a minor place in the etiology in spite of its widespread prevalence. Syphilis as a

coincident or direct etiologic factor was recorded in four cases in sixty-four reports where cause was cited—6.3 per cent. In only two of the 164 cases reported by Davis and McGee was there a positive response to Wassermann and Kahn tests—1.2 per cent.

Hofbauer experimentally produced a state allied to ablatio by the injection of histamine into pregnant animals, though at the Chicago Lying-in Hospital his findings could not be corroborated.

*Toxemic Types.* These must be presented collectively as it is not known whether the varying intensities are due to differences in the amount or virulence of a specific poison, or to a number of diverse intoxicating substances. A profound stimulus was given to general nosology, and to obstetrics in particular, when Brown-Séquard and his disciples promulgated the new theory that diseases could be engendered by noxious substances elaborated within the body. Toxemia, however, was not a new term, for obstetricians used it nearly a hundred years ago to designate a poisoning, not from ingested substances: the word was as comprehensively applied as the obsolete "miasm."

A second great contribution came with the development of the knowledge of endocrinology. As fantastic beliefs were sifted out by earnest investigators, hypotheses were evolved that toxemia was the result of aberrant metabolism, and to this, later, was added the influence of normal or abnormal internal secretions. We know the profound influence of thyroid and pituitary extracts upon ovarian function and upon the whole ovarian and uterine cycle. Malign mutations might be carried into the whole reproductive process. The ovum, and later the fetus and placenta, may have their own endocrine and metabolic by-products which may have a warring effect on the maternal host and her biochemical reactions. The nebulous theory of the protein reaction of the fetus upon the mother is indicative of this. It must be true that the fetus and the placenta may acquire disease and degeneration independ-

ent of the mother which will be adverse to the maternal welfare, as the reverse is indubitably true.

Time only will show the value of our theories. New hypotheses will be developed and discarded. Old notions will be revived as their tenableness is verified. Who would believe that the denial of Fehling (1887) that infarcts were *germaine* to ablatio would redound to his discredit, and that it remained for Bartholomew and Colvin to show that certain forms of infarctions were definitely correlated to toxemia, with special association to toxic placental detachments? This is a real progress even though the exact correlation between them has not been conclusively defined.

A new impetus was given to the study of the causes of placental detachments when Hennig (1875) demonstrated the presumed connection between them and albuminuria. Winter (1884) and Weiss (1894) substantiated Hennig's postulate by reporting cases where the two were coexistent. Lehmann (1899), cited the report of Rousseau-Dumarcet showing albuminuria in eleven of twelve instances of detachment, and in twenty-four of thirty-one examples of detachment in the Clinique Baudelocque. It was epochal when Desmond (1857) and Weiss (1894) recognized the ecchymotic spots on the uterus, though it became the honor of Couvelaire (1911) to interpret them correctly.

It has been alleged that chronic nephritis gave a woman a relative immunity against a possible placental separation. Williams, Frankl and Heiss, and Davis and McGee respectively stated the incidence rates to be 3.5, 3.9, and 9.6 per cent. The New York Lying-in Hospital in 1934 reported a frequency of 1.38, and in 1937 0.82 per cent for chronic nephritis. The assumed security of chronic nephritis against a placental detachment is not verified by facts. *Eclampsia* has been declared akin and even identical with toxic placental separations. It was assumed that under different circumstances the poison had a peculiar selective action, on the liver in the one, and on the uterus in

the other. In the combined collection of Goodell (106 cases) and of the writer (200 cases), J. T. Ingleby, J. L. Baudelocque, Hennig and Tucker reported the coexistence of detachment and eclampsia. The writer presented two instances of eclampsia-ablatio in his twenty-two personal cases. The combination occurred 6 times in 328 cases, or 1.8 per cent. In the sixty-seven cases of Couvelaire uteri collected by P. Willson (1922) the double disease was noted in six, 8.6 per cent. Harrar found the duality in 1 per cent, Davis and McGee in 0.61 per cent. In 1922 the writer stated, "It is plausible to believe that the concomitant presence of eclampsia and toxic ablatio is a manifestation of the activity of two foreign substances arousing diverse syndromes."

#### PATHOLOGY

The pathology may vary macroscopically and microscopically from normal or insignificantly changed placental values to slight mutations of the placenta and uterus, or to such extreme changes that even distant viscera are markedly altered. A retroplacental clot is almost invariably found, irrespective of the etiology. The absence of old black clots, expelled with the placenta, strongly indicates that an error of diagnosis has been made. If the egress of blood is mechanically prevented, free sanguinous fluid bathes the clot, and commonly is discharged with the placenta, at least in part. The clot is either free in the uteroplacental cavity, sessile and adherent to the maternal surface, or, if the periphery of the cavity has remained adherent for a sufficient time, the coagulum will fill a depression on the maternal surface of the placenta. While the clot is distinctly fresh it is soft, compressible and of normal reddish appearance. As time elapses it blackens, contracts, extrudes its serum, and becomes firm. The independent studies of Rokitansky and Spiegelberg and Brodhead have demonstrated that not infrequently similar but smaller clots will be found in mature placentae as the result of unmani-

fested slight hemorrhages long antedating the labor. Spiegelberg found them present in fifty-seven of 5,900 inspections, Brodhead in seven of 1,000 placentae examined at term. One or many such clots may be distributed over the maternal surface, varying in size from a millet seed to considerable dimensions. In one case a woman was severely hit over the uterus, collapsed, was revived and went to term. Here the clot was the size of a goose egg. These clots, having endured for a protracted period, are very firm, the color of dirty putty, due to the absorption and disintegration of the hemoglobin. Separations and hemorrhages, it is believed, result from isolated degenerative changes in limited areas.

In cases of trauma, or inflammatory or degenerative processes, comparatively little illuminating change is present. At times the appearances of the uterus and placenta are those normally present. However, gross cellular morbidity may be revealed. The infarctions may be more pronounced than normal. They may vary in color from old white to comparatively new areas in which the hemic elements are still in early decomposition. The reddish to white infarctions may be large and cover a considerable portion of the maternal surface, or may even be buried within the placental tissue. Placentitis may be recognized by a profusion of capillaries undergoing thickening and thrombotic obliteration. The serotina is likewise thickened. There may be connective tissue proliferation, showing a variability in the development of sclerosis.

*Toxic Pathology.* The diverse pathologic changes in the tissues of women seized with toxic ablatio leads to the conclusion that there are at least two distinctive noxious substances which produce different types of toxemia, one the ordinary form, the other the Couvelaire type. It is hardly tenable to hold that diverse effects are the consequence of a single element varying in virulence, even though we have not clearly differentiated the two clinical types.

In ordinary toxic ablatio, the kidneys are generally involved in varying degrees.

Albuminuria, casts, and some hematocyturia are expressive of an acute nephritis. Microscopic specimens show involvement of the cortical layer and the glomeruli. The liver rarely reveals special alterations beyond a possible cloudy swelling. The gross appearance of the liver is unaltered. Microscopic study of the placenta may show normality or hypertrophy of the vascular intima, with, perhaps, a connective tissue proliferation. These are particularly evident adjacent to the placental site. The placenta contains a number of infarcts of recent origin, brown or brownish in color. The white ancient infarcts are present in nearly all normal placentae, but in ablatio may be larger. They may be on the maternal surface or buried within the structure. In a few instances the escaping blood has a port wine hue, and is watery with little or belated coagulability.

*Uteroplacental Apoplexy.* The poison produces extreme permeability of the vascular supply of the affected organs, with widespread hemorrhages, thromboses, or extensive penetration of free blood in the tissues. Extremely rapid coagulation results after the blood has escaped the vascular intima. Extreme hemolysis may occur at one point, and retention of normal characteristics at another. Cellular lysis, wherever the blood bathes the tissue, and marked leucocytosis occur with great predominance of the polymorphonuclears. There is a dearth of literature on blood analyses of toxic patients in whom premature detachment is likely or has actually occurred. Hemal studies prior to the explosion and afterward could elucidate many moot problems. Ultimate knowledge of etiology will be as certainly discovered from clinical investigations of the blood as from shed specimens or from tissues obtained post-mortem.

In 1923 the writer reported a case of toxic apoplexy, in which the placenta and uterus had a wide distribution of polymorphonuclear leucocytes, not only in the fetal and maternal blood streams, but also in the extravasated blood. Unfortunately



blood counts had not been made before operation. Since then we have taught that the blood examination should be a routine part of the antepartum investigation. Serial study of numbers of cases would tend to prove whether polymorphonuclear leucocytosis is a peculiarity of toxic apoplexy alone, or present in all ablatios. If it is limited to the toxic apoplexy, a valuable diagnostic aid would be available. If it is present in all premature detachments it would resemble the state obtaining in ruptured ectopic where the white count may rise to 15,000 or even 40,000.

The kidneys are almost invariably involved. There is a high grade cortical degeneration, thrombi are often found, and the glomeruli and the tubules are markedly impaired. The thrombotic process may be so extensive that in a few instances the cortices of both kidneys have been entirely disintegrated. The liver may present corroborative evidences and subperitoneal hemorrhages, from petechia to those of material size, may be present. These retroperitoneal hemorrhages may appear elsewhere in the abdomen, but they are always superficial extravasations. In the loose areolar tissue of the broad ligaments or beneath, hematomatous formations are sometimes noted, though they are exceptional. Within the liver there are hemorrhagic infiltrations distant from the portal areas. Necrosis is not invariable. These hemorrhagic spots are clearly distinguished from those seen in eclamptic liver degenerations.

The gross appearance of the uterus is extremely characteristic: the subperitoneal surface is blue-black to purplish in color; the ecchymotic splotches may cover large areas of the organ, or they may be small and multiple; they rarely are regular in outline, but rather are peculiarly rimmed with digitations. The variations in extent probably reflect the intensity of the venom. The adnexa may or may not be involved. In some instances the peritoneal surface is striated from superficial rupture of the serous coat. Serous fluid or free blood is rarely found in the abdominal cavity. The

cut surfaces of the uterus reveal wide diffusion of the extravasated blood, particularly in proximity to the placental site, and under the peritoneum and mucosa. Microscopic examination reveals the extensive diffusion of blood. In one place large muscle bundles are separated by massive extravasations, while in others, the fasciculi are bathed in blood or individual fibers dissected from one another by the blood. The intima of the vessels is thickened, the vessels may be filled with liquid blood or there may be thrombi. Wherever they may be differentiated, as in the writer's case, the polymorphonuclear leucocytes are greatly increased, even proportionate in number to the erythrocytes. The connective tissue may show some feeble attempts at proliferation, and the cells of the muscle tissue exhibit the effect of a cytolytic action.

The placenta may be extremely involved. Fresh infarcts, black to brown, may compromise extensive areas, so that in some cases considerable portions of the placenta are affected. The infarcts are more fragile than the contiguous normal tissue. On microscopic examination the same blood extravasations are apparent. The larger vessels may be distended with free blood, which later is coagulated. The capillaries have the same relative appearance, with, now and then, ruptured walls. The cellular tissue is thickened and undergoing degeneration. The rupture of the vessels, if the serotina is torn, may contribute the thought that the primary retroplacental blood is maternal with some admixture from the fetus.

#### MECHANICS OF PLACENTAL SEPARATION

The repercussion resulting from an injury may well be the cause of a loss of continuity of the uteroplacental union, the cavity thereupon becoming filled with blood. This hardly can be the case where the causal factor is of the pathologic or toxic types. Under these circumstances the apoplexy in the serotina is primary, the escaping blood forming its own antrum, unless we may conjecture that the diseased

area has so degenerated that there is a primary disjunction. If the disrupted area is central and the surrounding serotina normally adherent, the physiologic adhesion effectually dams the effused blood. The blood becomes a foreign body and stimulates uterine contractions. Contractions tend to diminish the capacity of the cavity, but acting upon the incompressible blood and clot, will force the latter to burrow its way afield. During each interval of relaxation additional blood will enter the cavity. Progressively, in this wise, supplemental separations occur until eventually the open space reaches the periphery.

All this time the bleeding is entirely occult and thereafter other factors may maintain the concealed hemorrhage. The first of these is a firm adhesion of a dense chorion, possibly the sequel of an endometritis. The second factor is that the membranes may rupture adjacent to the placenta, and the blood mingle with the liquor amnii. This putative cause of retention is hypothetical, as the opening has not been observed. However, when the membranes rupture at the os, free blood and clots are coincidentally expelled. Again, the presenting part—head or breech—may be so firmly depressed within the cervical ring that it serves as an effectual barrier. This is a constant factor, as frequently blood is discharged with the expulsion of the fetus and placenta—conclusive corroboration of antenatal separation. Again, a few examples of *conglutinatio orificii externi* have been reported which prevented any overt hemorrhage. Finally, in some examples of the *Couvellaire apoplexy* the blood coagulation is so prompt that there is no free blood to escape. Such are the dynamics of total concealment of the hemorrhage, which must be interpreted as the first cycle of uterine hemorrhage incident to antepartum separations.

The second phase of the hemorrhage is when blood escapes from the vagina. This may occur immediately in relation to the appearance of the primary symptoms, or may be delayed for many hours. The first

sign of external bleeding may be manifested in one of two ways, dependent upon the interval between the onset and the time when a canalization has developed between the detached placenta and the internal os. If the interim is short the bleeding may appear as a seepage, or it may be of material amount expressed by free blood or clots. If the interval indicates considerable chronicity, the restrained blood coagulates, the clots contract, extruding the serum which finds its way to the os, appearing as a pinkish fluid which may be scanty or profuse. In one case of the writer's, it was so abundant that it saturated the underwear and dress, so that the attendant deemed it to be liquor amnii: such serous discharge was noted in five (23 per cent) of his personal cases; in the compilation it was recorded in twenty-two (11 per cent). Careful observation will determine this evidence of internal bleeding far more frequently than is generally supposed. In due course free blood will follow the serous discharge.

Finally, the onset may be so precipitous that a massive separation and a hemorrhagic deluge may take place before succor can be of any avail.

Two anomalous forms of premature detachment are worthy of mention; that of separation, prolapse, and extrusion of the placenta before the fetus, and complete thrombosis of the sinuses with separation but without hemorrhage. Feinberg, Hüter, Anderson and Haberlin reported such examples and Feinberg and Münchmeyer each cited a case of the latter.

#### SYMPTOMATOLOGY

Some authorities have described an array of symptoms which are supposed to be characteristic of a typical ablatio. It would be caviling to question the evidence that in some instances pronounced signs and symptoms are unequivocal, but these are classical examples from which must be evolved the symptom complexities which accompany aberrant courses. One case may

be recognized instantly, while in others hours may elapse before a true conception is reached. The most bewildering implications may appear during the early hours, and then some final special signs will develop which permit a conclusive diagnosis.

The symptoms of retroplacental hemorrhages are protean in their manifestations, varying under diverse conditions and circumstances. The mutability of the criteria of ablatio offers a striking contrast to the signs of placenta previa. Both follow placental separation, both have hemorrhages, yet the hemorrhages of ablatio produce an array of startling reactions while those of previa produce but one—anemia. A minimal separation with blood restrained within a ring of firm adhesion will pass unnoticed, or, at most, will produce only vague transitory discomfort, while pregnancy continues unaffected. This may not be considered a clinical type.

A practical elucidation delimits three groups: (1) the mild; (2) the severe; (3) the fulminant. Each of these may be subdivided into absolutely and relatively concealed hemorrhages and again into partial separations and complete disjunctions of the placenta, and finally into etiologic types, as traumatic, nontoxic, toxic, and the Couvelaire uteroplacental apoplexy. Each primary group, from mild to fulminating has increasingly obvious signs and symptoms, though certain dominating characteristics may be in abeyance in individual cases.

All the manifestations of ablatio emanate from the retroplacental hemorrhage, producing local reactions or systemic effects. As the amount of bleeding is always masked, both before and after external showing, the amount lost may be judged in relation to the circulatory effects and by the general facies. The depictions are for the average woman; deviations in weight, physical condition (the large healthy woman may stand more, the weak, sickly, anemic one less). The cardiovascular system reacts more quickly to a slow bleeding, and more readily fails with severe gushes.

*One Pint Loss.* The prolabia and the conjunctivae are pale. The cutaneous surfaces show little or no pallor, and are warm. The pulse volume is of good quality, though the rate may be accelerated 10 or 20 beats; blood pressure readings may show some depression, respirations are unaffected or slightly faster. If erect, the patient may feel dizzy, but this is absent if she is lying down.

*Two Pint Loss.* The prolabia and the conjunctivae definitely lose all color, the skin is whitened and cool to the touch, especially in the extremities. Drops of perspiration appear about the lips, below the palpebra, and upon the forehead, and the skin generally is damp. The patient complains of faintness and may have repeated syncope. Nervousness is evident, even some restlessness. The pulse rate is materially increased—140–160, and its quality is soft and compressible. The blood pressure is distinctly lowered, both diastolic and systolic being 10 to 20 or more points below earlier readings. Respirations are clearly accelerated, and the patient complains of aches throughout her body, repeatedly mentions her weariness and experiences intense thirst.

*Loss of over Three Pints.* The exposed mucosa is colorless, the skin cold, clammy and alabaster or even waxy, much of its elasticity lost. Beads of perspiration appear about the head. The pulse is thready and extremely rapid, over 200; the diastolic pressure is extremely low, with feeble rises of the systolic; respirations are increased greatly, to 40 or more per minute, and are irregular with the accessory respiratory muscles labored. Facial grimaces and contortions as air hunger supervenes are distressing to the bystanders. Thirst is imperious. The woman is extremely nervous, restless to a high degree, clamoring in her delirium, jactations will be pronounced. Throughout the ordeal she complains of the pains throughout her body.

The signs and symptoms are here discussed in the order of their importance rather than in the chronologic order; in

fact, the latter would be impossible as many of the diagnostic features appear synchronously.

*Systemic Reactions. Faintness, Dizziness, Syncope.* Their presence is dependent entirely upon the amount and the suddenness of the blood loss and the response of the sensorium. The manifestations may be temporary or persistent, but their significance is greater than their apparent intrinsic worth. The laity holds a high opinion of the lack of stability of the average pregnant woman, and tends to believe that such cerebral imbalance is a phenomenon peculiar to her condition. From the frequent belated diagnoses one must infer that some physicians also disregard this sign, which may be ominous. Every physician should determine promptly the basic cause for the cerebral anemia before he commits himself to its innocence; syncope may be the only symptom of rupture of the serotina obtainable until the patient regains consciousness. Before this time the physician must investigate the uterus.

*Nausea and Emesis.* These are other symptoms which are popularly regarded as normal characteristics of the pregnant woman. When they are associated with dizziness and syncope they warrant an especial endeavor to differentiate them from the supposed normal and from abdominal disturbances. The combination demands an examination of the uterus, as otherwise the opportunity for making an early diagnosis of detachment will be lost. In one case these signs were the only tangible evidences, and nearly ten hours elapsed before conclusive symptoms were sufficiently developed to permit a diagnosis.

*Direct Evidences of Hemorrhage.* The facies of the patient strongly indicates the possibility of hemorrhage (*vide supra*). The pulse rate, and a soft, compressible pulse also offer some suggestion. The enumeration of the erythrocytes and leucocytes, and the estimation of the hemoglobin content are vitally important. These data will be in the normal range if the first tests are

made promptly after the onset, but are indispensable gauges for comparison with later serial examinations, hour by hour. The primary effect of hemorrhage is to reduce blood volume *only*; progressively, as the bodily sera are taken into the blood stream the proportionate cellular elements diminish directly as dilution increases.

*Blood Pressure.* The taking of blood pressure is an essential part of sane prenatal and intranatal maternal care. The lamentable thing is that too often this essential diagnostic detail is absent from reports. A mitigating circumstance is that a large majority of ablatios are admitted to the hospital in full flower. Yet, little or no mention is given to the interpretations of blood pressure. In two classic contributions on the several types of ablatio published within recent years, no comment is made concerning the use of the sphygmomanometer in one, and the other disposes of the matter in three lines. The writer (1923) stated: "It would be eminently desirable to have more recording of blood pressure readings in relation not only to the toxic types of placental separation, but in ordinary ablatios as well, for they may furnish valuable clinical data for the differentiation between them."

The sphygmomanometer is an essential appliance in all obstetric work. It is as invaluable when conscientiously used in the presence of possible or actual hemorrhage as it is in toxemias. In ablatio it serves a dual purpose: its routine use during the course of hemorrhage demonstrates the effect of the blood loss upon the circulation and in all types of ablatio where the blood is blindly stored up within the uterus it offers a better criterion of blood volume and content than any other measure. A falling blood pressure is an infallible index of continued bleeding and is the quickest means of determining the response of the body economy to proper stimulation.

Secondly, at least half of all ablatios are in some measure toxic, and blood pressure *may* give some conclusive evidence of the degree of the toxicity. This is true, even

though the next sentences are paradoxical. We are still in the dark as to whether the toxemias of ablatio are necessarily accompanied by a hypertension. True, most clinicians make the basic diagnosis of toxemia on the high pressure (over 140, systolic) and the urinalyses. The large majority of toxemic ablatios are first seen when the patients are institutionalized, and they will quite generally have hypertension. In contrast to this, some toxic types, as well as the virulent Couvelaire apoplexies, will have a normal rate or have hypotension. Couvelaire states that toxic apoplexy is not necessarily correlated to vascular lesions or hypertension. It is still a moot question whether this is due to absence of increased tension or to the depressive action of the loss of blood volume. P. Willson (1922) collected sixty-seven examples of the Couvelaire type from the literature: of these only nine reports had records of pressure readings; two were normal (100 and 120), and six had a range from 160 to 260 (160, 170, 174, 180, 200, 260), the patient with 280 having a coincident eclampsia. The writer's case of Couvelaire uterus, proved by cesarean section, had a pressure of 120.

To restate the facts—the routine and conscientious use of the sphygmomanometer will supply us with fundamental knowledge of the connection between hypertension and all types of ablatio, both nontoxic and toxic.

*The Uterus.* All the rest of the signs and symptoms of ablatio emanate from the actions and reactions of the uterus and its contents. The whole behavior of these structures depends upon the response to the stimuli created by the intra-uterine bleeding. The restrained blood promptly becomes a foreign body. A small area of the placenta having separated with a minimal bleeding, there may be minor discomforts to the patient, but abnormality in connection with the uterus may be ignored. A major separation with a material gush of blood will usher in a train of violent reactions; the woman may be conscious of the

distention going on and it has been reported that the by-standers have seen the uterus increase in size. The pain may range from the sensation of a distention to such a degree that the woman will clamor about it. In some few instances the concussion of a large, or total, separation may produce a rending pain which is comparable to that of the rupture of the uterus or of an ectopic pregnancy. A placenta which is located lower on the uterine wall, with its lower border separated may produce no distress whatsoever—it may readily be mistaken for a lateral placenta previa. On the other hand, a central separation or detachment of the upper border may be accompanied by a massive outpouring, violent pain, and classic findings. In the report of Davis and McGee *no pain* or contractions were noted in 8 per cent of the 164 cases. Pain is proportionate to the degree of separation, reaching its maximum with total separation. The uteroplacental apoplexy, where total separations are the rule, almost invariably produces pain.

Examination of the uterus divulges many important facts. *Tenderness* of the uterus, especially in the region of the placental site, is often found, though according to Davis and McGee, it is elicited in only 30 per cent. Where the uterus is distended with the major portion of the placenta separated tenderness is particularly noted. It is important to note the *consistency* of the uterine wall. In the author's 200 cases facts pertinent to this point were given in forty reports (twenty-two as tense, eighteen as boggy). The authors above cited state that tenseness (ligneous hardness) occurred in 29.2 per cent. It is still a moot point whether we should or should not reserve extreme hardness for the Couvelaire type.

The *contour* of the uterus should be observed by inspection and palpation. If there is wide diffusion of the blood it may be ascertained that the uterus is symmetrically enlarged with the normal ovoid. If the placental site is anteriorly placed (which occurs in about half of all pregnancies), and the blood is confined in a

circumscribed mass, there may be a marked irregularity, even a definite protuberance—always sessile—the *accessory tumor* of the

patient often perceives violent fetal movements for a moment, followed by the quiescence of death. If the physician sees

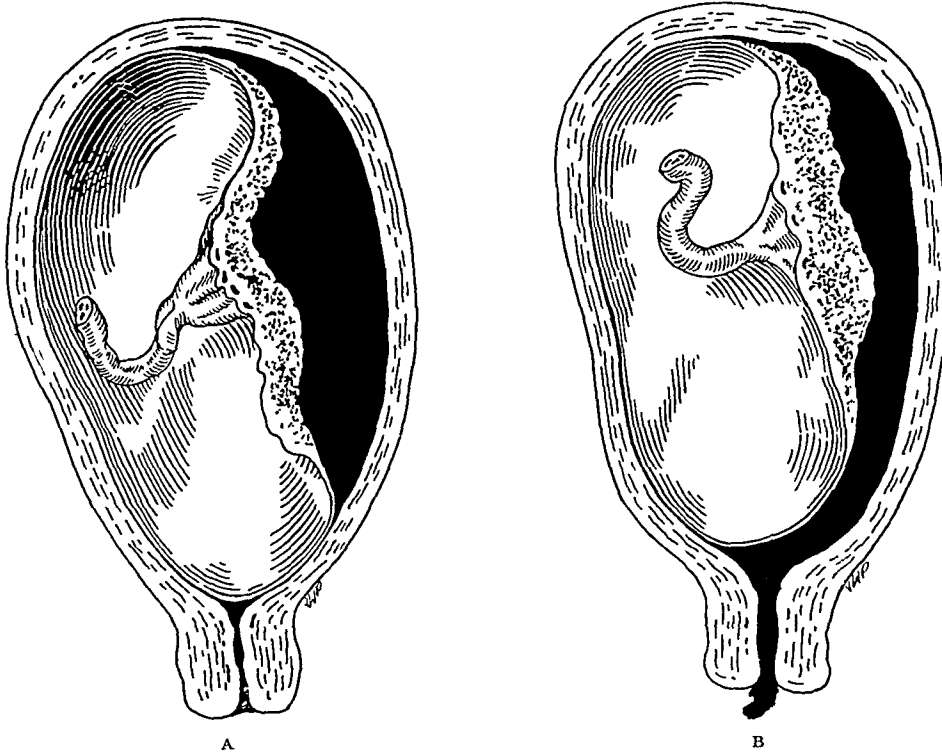


FIG. 1. Ablatio placentae. A, internal or concealed hemorrhage. B, combined internal and external hemorrhage. (From Holmes, in Davis' "Gynecology and Obstetrics," Prior.)

old writers. This is a characteristic finding, but must not be confused with a subserous fibroid. The tumor was recognized in fourteen cases of the writer's assembly—7 per cent; in his personally observed cases (twenty-two) it was noted in five (22.7 per cent). This sign possibly might be observed with twice the frequency if the posterior wall were palpable. If the placenta and clot are in a cornu, with the fetal pole in the other horn, a bicornuate uterus may be simulated.

*The Fetus.* After separation has occurred, a malposition is found in about 10 per cent of women, the fetus being crowded from its axial relations by the clot and dislodged placenta. A minor placental dislodgment allows the fetal heart rate and quality to be normal, but in material separation the heart tones indicate the fetal jeopardy by their gross irregularity and quality. Slow death ensues. If the separation is massive or complete, the

the patient early, the manner of eventual cessation of fetal heart tones may give some slight notion as to the degree of placental separation. The fetus in any case dies from asphyxiation, from the toxemia if present, and possibly from hemorrhage if the placenta is torn.

*The Hemorrhages.* Certain statements may be accepted as axiomatic. The total concealment of the blood is an inherent primary attribute of the diseases characterized by placental separations, irrespective of the generic name designated by the fancy of the user. The condition may result from trauma, pathology, of peculiarly local form, or from systemic dyscrasia as toxemia or uteroplacental apoplexy. The concealment is due to definite physical barriers which may be present in all intra-uterine hemorrhages, irrespective of cause, not alone in ablatio, but in certain uterine ruptures and in a few disintegrating submucous fibroids. If there are no barriers,

the hemorrhage of an ablatio may become external promptly, while if barriers exist, the concealment persists until uterine

the blood discharged prior to delivery. We cannot subscribe to a classification which would include "all cases where the bulk of

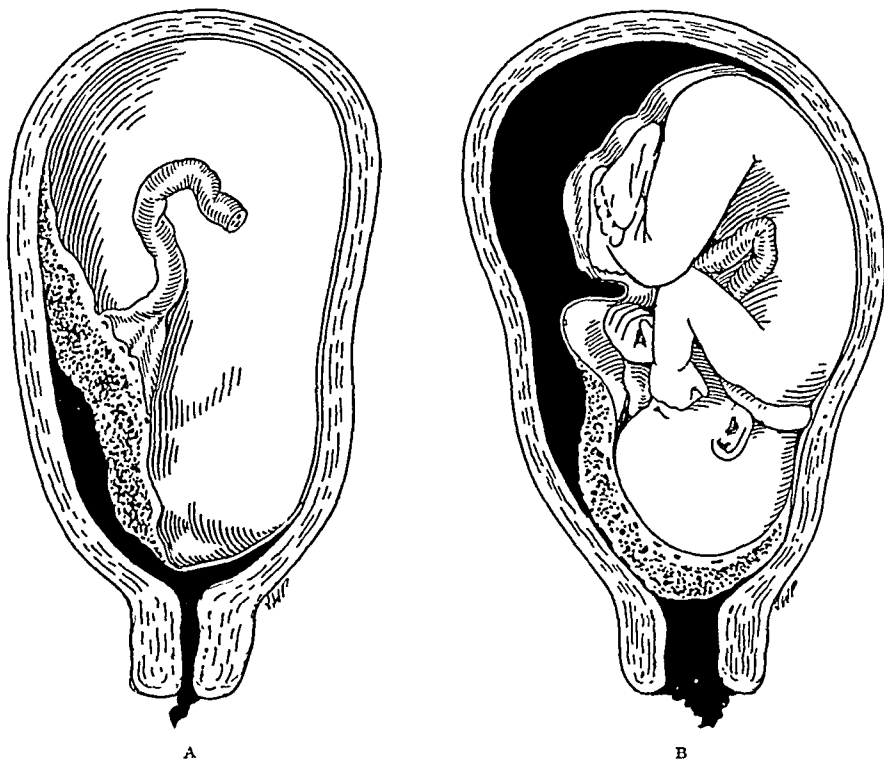


FIG. 2. Ablatio placentae. A, external hemorrhage. B, external hemorrhage and prolapsus placentae. (From Holmes, in Davis' "Gynecology and Obstetrics," Prior.)

contractions or other mechanical processes raise intra-uterine pressure, thus destroying the barricade.

*The external bleeding is merely a tardy corroboratory sign of the intra-uterine events comparable to the appearance of jaundice in liver disease or late hemorrhages in typhoid. It should be emphasized that there is not one sign or symptom present in totally concealed cases which does not appear in the patent types—except that the latter gives ocular evidence of blood. The external hemorrhage under no circumstance is the gauge of the amount of blood stored within the uterus. As a corollary to this we have an invariable diagnostic point, which substantiates all ante- and postpartal diagnostic features; with the child and placenta are expelled all the free blood and clots which were pent up in the uterus. The extruded blood is in inverse proportion to*

the hemorrhage was retained within the uterus are internal hemorrhages." We do not have positive criteria upon which to base the estimate of the amount of retained blood.

From the time of Goodell it has been believed that totally concealed hemorrhages carry a heavier toll than the open. The high mortality rate of "concealed" cases is not due so much to the fact of complete retention, as it is to the hours of needless waiting until a correct diagnosis is made. On theoretic grounds the complete retention of blood is nature's endeavor to conserve life, for the blood is dammed up. This is favorable if there is tonicity of the uterine muscle. The success, and it was an actual triumph in its era, of the Dublin method of treating accidental hemorrhage by vaginal tamponade relied upon this—converting a patent hemorrhage into an

occult one. The writer suggested the division into relatively and absolutely concealed hemorrhages, but such clinical forms

#### DIAGNOSIS

The introductory sentence in the discussion of ablatio expresses the conviction of

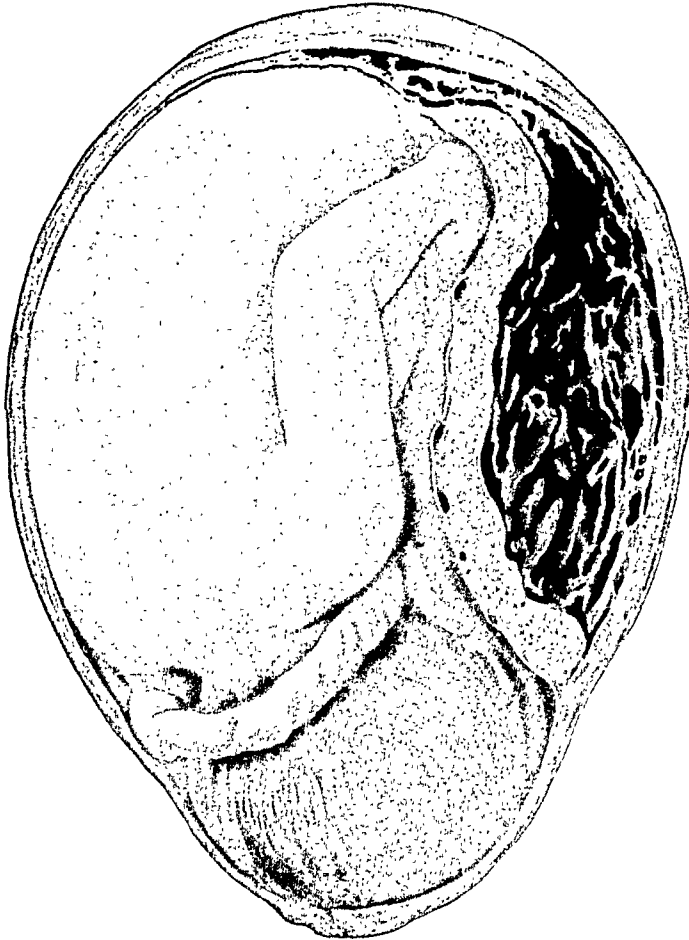


FIG. 3. Premature separation of the placenta with concealed hemorrhage. The uterus was removed by supravaginal hysterectomy, owing to the marked involvement of the uterine muscle. Williams' specimen. (From Holmes, in Davis' "Gynecology and Obstetrics," Prior.)

are not basic enough to permit their use for the computations of mortality rates. Too many factors, some clearly featured, and others too obscure for interpretation determine the death rates. The amount of blood lost, within the range of practical reason, does not always determine the cause of death. On the average the hemorrhages in traumatic and pathologic ablatios are excessive, yet we know the mortality rates for them is low. We know that the usual hemorrhage in Couvelaire's uterus is remarkably and relatively small, yet the mortality rate is high, because a malignant toxic substance saturates all tissues.

the writer that we are not dealing with a specific disorder, but rather with a number of morbid states which are expressed by two fundamental crises—placental separation and concomitant hemorrhage. Subsequent actions and reactions are dependent upon the degree of placental separation, the location of the placental site, the amount of blood loss. The etiologic factor probably alters these influences as much, if not more, than the nervous and physical stability of the patient. There is such diversity in response to the separation per se and in the hemorrhage, that future clinicians will perhaps be able to unravel



the doubt by means of these differences. As it now is, generic ablatio has a kaleidoscopic presentation which is truly perplexing, varying in the same patient and in different patients. It must be recognized that a composite photograph is only exceptionally seen, as details will be present in one case and not in another, and the intensity of each evidence is very variable. However, that we may have prototypes of premature detachment we present these imaginary but graphic examples:

The woman may be asleep or concerned with her varied duties while in pregnancy or in labor. Suddenly she feels an abdominal discomfort, indefinitely located or limited to the uterus. She becomes dizzy, and soon regains her equilibrium. Nausea may or may not be present. If she is in labor the contractions increase in vigor and pain persists in the intervals between contractions. Again, after a period of unrest, all symptoms may subside and in the course of time labor begins. If the bleeding is sufficiently ample, whitening of the mucous membranes appears, and even the skin is blanched to a degree. The fetal movements may be clearly perceived, but finally they disappear. The physician comes; he corroborates the evidence of an anemia by repeated blood examinations, notes some tenderness, and if the small hemorrhage is restrained within the bounds of a uteroplacental cavity, he may note the the uterine protuberance—the accessory tumor. If the separation is limited the fetal heart tones may be variable, from normal to marked irregularity, and rapid; if there is an extensive separation the fetal heart is inaudible and fetal movements will have ceased. The uterine consistency may be little altered. After a variable period there may be a pinkish serous discharge, followed later by the escape of dark old blood, even black firm clots. The temperature falls, the amount depending upon the volume of blood loss; in this type of separation the blood loss is commonly not great. Also depending upon the blood loss, the blood pressure may be depressed. Urinary

examination may not show any abnormality, or there may be some evidence of an acute nephritis—traces of albumin, few casts. This is the picture in mild to fairly severe cases, which may result from trauma, from purely localized pathology of the uteroplacental union, or some toxemias of lesser severity. In contrast to these manifestations we have the other extreme:

The patient may have had a known nephritic involvement, with some hypertension—or this may have been unobserved. Without premonitory signs she is seized with an agonizing pain, described perhaps as a bursting pain. She collapses and may be unconscious. The mucous membranes are without color, the skin dank and of waxy whiteness. She may be in deep shock. The pulse rate is very rapid and of poor quality. Serial blood counts show a high grade anemia. Whatever the blood pressure may have been prior to the attack (hypertension), it is now distinctly depressed. The physician finds the uterus symmetrically enlarged or showing marked deviation in contour. The patient, when revived, tells of tumultuous fetal movements for a few moments, then quiet. The malposition of the baby may be discovered if the uterus is sufficiently relaxed, but in other cases the tension is so great (tetanic contraction) that nothing in utero is palpable. Tenderness pervades the whole uterus, especially over the placenta. Appalling external hemorrhage may appear or there may be no showing for a protracted period. Finally, there is a profuse discharge of the serous fluid (blood serum extruded from the clot) sometimes of such quantity that it is mistaken for liquor amnii. Later, slight to profuse discharges of old black blood interspersed with old clots are in evidence. Urinalysis usually shows definite albuminuria, casts erythrocytes and hemoglobinuria, varying with the intensity of the toxemia.

So far as now known, uteroplacental apoplexy does not offer any clinical intimation of its existence. It is entirely theoretic but we may predicate its existence if

symptoms are out of all proportion to the amount of blood loss. As the placenta of this group is almost invariably entirely degenerated, the violent onset is accompanied by especially sharp uterine turmoil—pain to an extreme degree, and often, though not invariably, an excessive rigidity of the organ. One may be justified in considering that the placenta has been completely severed from its attachment. The hemorrhage of this form of toxemia is rather less than in other types. The bleeding is characterized by the sudden outpouring, then a remarkably quick coagulation; the later external bleeding may be negligible, hardly spotting, and rarely will there be a postpartum hemorrhage. These symptoms are in sharp contrast to the external gushing which may dominate the picture where a severe injury caused the separation. Couvelaire states that vascular lesions and hypertension are not necessarily a part of the trouble. Shock is often present. The correlation of a leucocytosis (polymorphonuclear leukocytosis) of the maternal circulation and its presence in the uterine and placental tissues deserves an intensive study. At the present time we may not recognize the existence of this condition (apoplexy) unless we inspect the uterus during a cesarean section or on the post-mortem table.

The third stage of labor will offer conclusive corroboratory evidences of the correctness of a diagnosis of ablatio of every type, or entirely negate the thought. The expulsion of old black blood and old clots with the fetus and placenta is so constant that their absence is indicative of a lateral previa.

#### DIFFERENTIAL DIAGNOSIS

The diagnostic difficulties in the interpretation of the phenomena included under the broad caption of premature separation of the normally situated placenta must be appreciated when the range spreads from those minor abnormalities which are recognizable only by inspection of the secun-

dines, through those which give extremely vague and transitory discomforts, on to those with marked symptomatology and high lethal crises, to uteroplacental apoplexy. J. Nevins Hyde, the eminent dermatologist, maintained that the mutability of syphilitic evidences was so great that there were few diseases which it did not resemble. In the same manner, the clinical expressions of ablatio have such vagaries that they may resemble other hemorrhagic disorders, or even simple alien manifestations.

Dizziness, faintness or syncope are inherent accompaniments of all losses of blood. In the past, and even today, too much stress is laid upon their occurrence as normal (!) reflections of the cerebral instability of the pregnant woman. By the same token, nausea and emesis are too lightly held to be features characteristic of the pregnant woman's gastroenteric unrest. Their occurrence demands that the physician shall not cease search for the basis for their inception. Too often the case reports demonstrate the quandary of the physician until he is enlightened by the external bleeding. In such cases sooner or later the blood picture will reveal the fact of a progressive anemia.

*Placenta Previa.* In previa the first sign of trouble is vaginal bleeding, but it may be one of the last evidences of ablatio. Both the hemorrhage of previa and that of ablatio may result from some seemingly trivial trauma. The uterus in previa is never abnormal in contour, unless because of malpresentations, and never is it increased in size. In ablatio the contour is frequently disturbed by concealed hemorrhage and if this is extensive the uterus is invariably increased in bulk. A vaginal examination will permit the discovery of the low placenta, and the textural changes incident to a previa. The placenta in premature detachment is never palpable. As previously stated, the line of demarcation between a placenta which approximates the area of the retraction ring, and one which definitely dips into it may not be

clinically demonstrable: if the lower border of the former separates as the latter (a high lateral previa) inevitably must, the hemorrhages may hardly be differentiated, for both will be without accompanying discomfort. As the appropriate treatment of both is the same, the distinction between low placental separation and high lateral previa is of no importance. Inspection of the extruded secundines will permit one to measure the distance between the chorionic opening and the placenta; if short it probably is a previa, if longer, ablatio.

*Uterine Rupture.* Rupture of the uterus generally takes place late in labor at a time when a few placental separations may occur. The complete dehiscence with the extrusion of the fetus into the abdomen hardly permits confusion of one with the other. However, incomplete destruction of continuity may cause confusion in diagnosis. The labor is prolonged, with gradually increasing pain between contractions, and more acutely perceived with them. The round ligaments, long before the accident takes place, are tender to the touch, tense and swollen. With rupture, pain greatly diminishes. Pain is almost constantly located suprapubically, and an obstructed labor is usually the cause. The pain of ablatio is high in the uterine wall, localized or diffusely perceived by the patient. In both, external bleeding may occur unless dammed back by the presenting part. If the uterus is completely torn through the escape of the fetus into the abdominal cavity, and sharp retraction of the organ occurs there is no difficulty; in the incomplete forms the uterus rarely increases in size, while in ablatio distention is noted.

*Acute Polyhydramnios.* The rapid accumulation of liquor amnii, usually during a period of days, sometimes in a few hours, never produces hemorrhage during the process. The uterus always is either piriform or spherical. Measures should be taken to prevent a rapid escape of the fluid, for there is danger of placental separation from sudden contraction and retraction.

### PROGNOSIS

The writer has expressed his conviction that generic ablatio comprehends at least four, if not more, distinct maladies. Each has its specific etiology and pathology with placental separation and hemorrhage common to all. Adventitious clinical signs and symptoms are *seemingly* possessed by all, but future investigators will probably evaluate them properly, producing a separate symptom complex for each. Three of these etiologic types have certain pathologic identifications, local or systemic, which permit a certain degree of differentiation. These three may have their onset precipitated by trauma. Injury alone may induce the catastrophe in the absence of local degenerations. Each type may be evinced by trivial signs, by marked reactions, or by most tumultuous unheavels. In our ignorance of fundamental principles there is no common standard for classification of types, of their symptom equivalences or contrasts, of the enumeration of the relative values of methods of treatment *for each*, or a means for the calculations of the respective mortality rates. All data must, more or less, be summarized collectively. Migraine, eye strain, and penetrating gunshot wounds of the brain have a common symptom—headache—but who would group these together for therapy or present a common mortality rate for the three. Any plan for the comparative study of mortality rates is fraught with inconsistencies, although certain trends are clear.

Irving has most graphically portrayed the influence of two of the etiologic factors. The Boston Lying-in Hospital had 224 instances of nontoxic ablatio with eight maternal deaths—3.5 per cent; 129 toxemic separations with ten deaths—7.7 per cent. It is not known how many Couvelaire apoplexies were among the latter, but we do know the mortality rate is materially higher than for ordinary toxemias. These same 353 cases were regrouped into external and internal hemorrhages; there were 234 examples of the former with four

deaths—1.7 per cent; 119 of the latter with fourteen deaths—11.8 per cent. Of the latter, Irving states that in "all but two of our cases of internal hemorrhage, there was some visible bleeding at some time." We question the advisability of this distribution, for a concealed hemorrhage is never patent. We would reiterate that the external flowing, whether large or small, is no criterion of the amount of internal accumulation. The delay in recognizing an absolutely concealed case must contribute to increased death rates.

TABLE VII  
MATERNAL MORTALITIES IN ABLATIO PLACENTAE  
Spontaneous Births and Conservative Management

Authority	No. of Cases	Deaths	Rate Per Cent
Weymeersch-Snoeck	853	56	6.6
Davis-McGee	330	18	5.5
Irving	204	1	0.5
De Snoo-Streink	214	11	5.1
Le Lorier	56	1	1.7
A. F. Maxwell	47	0	0
Solomons	25	1	4.0
Bland-Rokoff	414	16	4.1
Totals	2,143	104	4.9
Spanish Windlass with Rupture of the Membranes and Tight Cervicovaginal Tamponade			
Polak	16	1	6.2
Irving	16	0	0
Heffernan	7	0	0
Totals	39	1	2.6

The tonicity of the uterine wall is of some value in determining the maternal risk. A firm wall is more prone to react to stimuli since firmness tends to inhibit retention of an undue amount of blood. When relaxation is present the converse may be true. Of the 306 cases collected by Goodell and the writer, the status of the uterus was given in eighty-six; there were twenty-two deaths among the sixty-six women with tense uteri—33.3 per cent—and nine deaths in the twenty with relaxed uteri—45 per cent.

Irving's tabulation of mortality rates as influenced by intervention is most enlightening, for it utterly shatters every rule that all placental detachments be managed by radical or polypragmatic practices, such as routine cesarean section. Irving characterized the period when accouchement forcé was rampant as the "dark age" of modern obstetrics; the promiscuity with which cesarean sections were performed for nonsensical or spurious indications may be added to the reason for such a "dark age." In the heyday of cesareans for eclampsia

TABLE VIII  
MATERNAL MORTALITIES IN ABLATIO PLACENTAE  
Results from Cesarean Section

Authority	No. of Cases	Deaths	Rate Per Cent
Le Lorier	4	1	25.0
Weymeersch-Snoeck	227	47	21.0
Maxwell	8	1	12.5
Irving	99	11	11.1
Willson	21	4	19.0
Brodhead	8	3	37.5
Williams	10	3	30.0
Fitzgibbon	4	1	25.0
Siegels	11	2	18.2
Davis-McGee	29	4	13.8
Bland-Rokoff	107	12	11.2
Goethals	39	6	15.4
Totals	567	95	16.8

the writer repeatedly asked the opinion of general surgeons regarding the advisability of an abdominal operation on a patient whose kidneys were grievously injured by an acute nephritis, whose liver was in gross dysfunction from some lethal poison. The consensus of opinion was, "never," unless the necessity was so great that no other recourse were possible. Obstetric attendants have been slow in learning this aphorism. This has a direct application in connection with the treatment of ablatios. Irving puts it, "The most remarkable argument advanced by the proponents of cesarean section is that it affords an opportunity to perform a hysterectomy . . . The logic is not apparent which compels

one to perform an operation with a 20 per cent mortality, so he may convert it into another with twice the death rate." Tables VII to XI show the mortality rates under various conditions as presented by different authors.

TABLE IX  
MATERNAL MORTALITIES IN ABLATIO PLACENTAE  
Results from Supravaginal Hysterectomy

Authority	No. of Cases	Deaths	Rate Per Cent
Welz.....	3	1	33.3
Willson*.....	21	10	47.6
Fitzgibbon.....	3	2	66.7
Le Lorier.....	2	1	50.0
Maxwell*.....	1	1	100.0
Davis-McGee.....	6	0	0
Polak, Burgess, Bartholemew..	3	0	0
Holmes*.....	1	0	0
Totals.....	40	15	37.5

\* All proved cases of Couvelaire's uterus.

TABLE X  
MATERNAL MORTALITIES IN ABLATIO PLACENTAE  
Results from Pelvic Operative Delivery—Radical Treatment

Type of Interference	No. of Cases	Deaths	Rate Per Cent
Radical Treatment, Bland-Rokoff.....	284	38	13.4
Pelvic Operations, Irving.....	50	6	12.0
Brindeau-Lantuejol.....	18	2	11.1
Breech Extraction*.....	28	0	0
Craniotomy*.....	9	0	0
Forceps*.....	152	24	15.8
Version-extraction*.....	33	5	15.2
Vaginal cesarean section*.....	9	4	44.4
Maxwell.....	1	1	100.0
Hystereurynter*.....	57	7	12.3
Maxwell.....	10	2	20.0
Totals.....	651	89	13.7

\* Adapted from Davis and McGee. Bland-Rokoff reported six deaths after eleven attempts at forced dilatation—54.5 per cent.

The mother may die as the result of blood losses, largely from toxemia, from shock, and from sepsis. In the best of hands sepsis must destroy a few mothers, particu-

larly where antecedent manipulations have preceded entry to the hospital. The fetus may die from asphyxiation, possibly from hemorrhage through the torn placenta,

TABLE XI  
COMPARATIVE FETAL MORTALITIES IN ABLATIO PLACENTAE  
Resulting from Conservative Management, Cesarean Section and Radical or Operative Treatment

Methods	No. of Infants	Deaths	Rate Per Cent
Conservative Management			
Irving.....	241	102	42.3
Maxwell.....	40	10	21.3
Solomons.....	29	8	27.6
Bland-Rokoff.....	414	251	60.7
Weymeersch-Snoeck.....	853	522	61.3
De Snoo-Streink.....	214	166	78.0
Totals.....	1,791	1,059	59.1
Cesarean Section			
Irving.....	100	54	54.0
Maxwell.....	9	2	22.2
Bland-Rokoff.....	107	80	74.7
Weymeersch-Snoeck.....	227	175	70.7
Totals.....	443	311	70.2
Radical or Pelvic Operative Treatment			
Irving.....	16	15	93.7
Maxwell.....	10	7	70.0
Bland-Rokoff.....	284	207	73.0
Totals.....	310	231	74.5

certainly from toxemia, and prematurity. Goodell stated that detachments were responsible for the premature interruption of pregnancy in 50.5 per cent of all cases. Of 200 cases collected by the writer, in 157 the period when the symptoms appeared was stated: six were in the fifth month, four in the sixth, twenty-nine in the seventh, sixty-two in the eighth, and fifty-two in the ninth or at term. In other words, 64 per cent were premature. According to Irving forty-five premature terminations occurred among the 357 infants born—12.6 per cent.

#### TREATMENT

It is sufficiently evident that generic ablatio, comprising four or more unques-

tioned puerperal diseases, each of which departs itself with varying clinical intensity and different symptomatology, cannot have a routine management. There must be individualization of each case, and the method most suitable should be selected. Minor cases require the least interference compatible with the welfare of the mother. Fulminant ablatio requires an intervention which will decrease the gravity of risk, not an operation which will augment it. It would be utterly preposterous to maintain that cesarean section has no place in the management of certain placental detachments, but the suitability is restricted to a limited field. The nationally held notion that the abdominal route is the only solution is as false a premise as in eclampsia.

*Introduction.* The first prerequisite is that the laity should be educated to the precept that every little malaise may have its serious portent. They should call a physician early. And he should not rest until he has eliminated any and all possible underlying causes. Weymeersch and Snoeck state that intervention prior to a ten hour period carries a mortality of below 27 per cent; after that it rises to 40 per cent. Secondly, every patient must be given supportive treatment according to her needs. Blood transfusions are of vital necessity when the blood losses have been great. As a temporary expedient the parenteral or rectal administration of decinormal solutions may turn the tide. In the distinctly toxemic patient the salines and Ringer's solution will be of advantage in aiding elimination; glucose solutions are advisable in shock. Morphia in fractional doses is invaluable as an adjuvant where much blood loss has occurred, for the purpose of quieting the highly nervous woman. As the fetal mortality is exceedingly high at best, the fetal contraindication to the use of morphia is not valid. Finally, one must select that type of interference which guarantees the greatest safety for the mother. Above all things, select the method which shall be the primary, as well as the sequential pursuit.

Selecting one method and then turning to another is an obstetric blunder.

*Conservative Measures.* The expectant treatment has various modifications, introduced by various clinicians, but all have a common purpose in that drastic measures are entirely eliminated. The keynote of all variants is expectancy: a nurse must be in constant attendance; there must be frequent recording of pulse, temperature, blood pressure. The character of the contractions, changes in the nature of the pains, and tenderness of the uterus are noted. Frequent observations and palpations ascertain changes, if any, in uterine contour and size. The amount and appearance of the escaping blood are observed. The consensus of opinion is that the membranes are to be ruptured artificially, particularly if the uterus is contracting. In the absence of uterine activity, or even with its presence, fractional doses of a pituitary extract are given; nasal administration is more desirable as the plug may be removed promptly, if indicated. Any sort of massage of the womb is absolutely prohibited.

There is fair unanimity that spontaneous labor shall be awaited, and forceps employed only on definite indication when the head has descended deeply into the pelvis. Some would modify this by employing instruments as a prophylactic measure, but *high forceps should not be tolerated*. If the breech presents, as it will in about double the normal frequency, manual aid should be given or extraction, on indication only, after dilatation has been completed. During the hours of waiting such supportive treatment as is expedient should be administered. Some will routinely give saline solutions by clysis, even subcutaneously. Blood transfusions may be indicated in exceptional cases. This method is appropriate for at least 60 per cent of all types of premature detachment. The ultra-conservative physician will obtain happy results in a larger proportion than given above.

Some writers, by implication at least, would limit this method of treatment to

spontaneous labors alone, while others would include minor operative interferences, and others, apparently, would include forceps in the non-operative group, as they call routine forceps termination in normal labor as "spontaneous." For the more seriously compromised, the tampon and Spanish windlass treatment would be considered an extremely conservative measure as the results are nearly ideal. The use of the tampon was the time honored treatment for "accidental hemorrhage" in the Rotunda Hospital for over 100 years and was discarded by Bethel Solomons shortly after he assumed the mastership, as he left the mere rupture of the membranes, with indicated supportive measures, fulfilled every purpose. John O. Polak was so successful with the tampon combined with the Spanish windlass that Irving and Heffernan adopted the method to evade the cesarean operation. The technique is so simple that it is worthy of emulation. We must point out that the use of the tampon (or hystereurynter) carries a great inconsistency: every writer stresses the fact that absolutely concealed hemorrhages are more fatal than patent ones. Any type of plugging of the cervix or vagina converts an overt hemorrhage back to a totally concealed one. We have always maintained that the entirely concealed hemorrhage was more dangerous as it permitted procrastination before treatment could be based on a positive diagnosis. The paradoxical use of the tampon would seem to confirm this opinion.

*Hystereuryxis.* The rubber bag acts similarly to the tampon, but has the greater advantage in that there is more certain stimulation of the uterus and it will more surely arouse contractions, consummate dilatation more quickly, and more definitely prevent external bleeding. The one objection is that experience has taught that the intra-uterine bag is more prone to be followed by a septic death. In fact, sepsis vies with hemorrhage as a cause of the demise. The seeming ill effects (12 to 20 per cent death rate) probably would be largely

reduced if it were combined with the Spanish windlass. The membranes must be ruptured before the bag is introduced. However, on the returns, it would be preferable to use the tight tamponade.

*Extraction of the Fetus.* All statistics demonstrate that the best results obtain when spontaneous labor occurs. Therefore, it is desirable that no attempts at delivery should be assayed unless there is a clear indication. Those who practice the tenet that routine forceps are within the domain of spontaneous labor should discard the procedure for cases of ablatio. The same comments apply to extraction of the breech. High forceps connote an extraction through a partially dilated os, and should never be employed. Version carries its own risks, for it may cause an additional separation, just as its use may produce a primary separation. Version should only be done in transverse presentations, and on a *living baby*. On the dead, in early prematurity, or in the dying, decapitation or embryotomy should be done. The most remarkable feature elicited from a perusal of the literature is the paucity of cases delivered by craniotomy—in a condition with a fetal mortality of from 60 to 90 per cent. In the collection of the writer (1901), covering a period when craniotomy vied in frequency with forceps in some hospitals, there were but three craniotomies mentioned in 200 cases of detachment. In the recent literature only nine women had craniotomized babies. Times were when it was taught that forceps on a dead fetus was the height of violation of sound obstetric principles and the use of standard sized forceps on a premature fetus was a transgression. Yet there were twelve craniotomies recorded in an array of over 4,000 cases of a complication in which at least 2,400 dead feti were delivered, due to prematurity or asphyxiation or both! Under appropriate conditions cranioclasia is infinitely safer than forceps. We hold no brief for the abhorrent destruction of the living fetus, but we protest the esthetic fastidiousness which dictates an

irrational forceps operation on a dead baby when a craniotomy would be more scientifically correct and less dangerous to the mother. Cathala of Paris is the only one consulted who has dictated a similar teaching as the author. Vaginal cesarean section has a very small place in the operative treatment of placental detachments—the mitigating circumstances are very few. The blood bathed field seriously handicaps the technique.

*Cesarean Section.* This operation has been lauded the past years as the panacea for nearly all cases of placental separation by some writers of collated statistics who did not properly digest the facts. On the other hand, authorities who summarize wide experience demand that the procedure be limited to the few cases where other recourses are impossible.

Irving writes: "The woman with this form of internal hemorrhage [placental detachment] is not only handicapped by acute blood loss, but she is often the victim of shock—in three-fifths of the cases toxemia is present . . . accompanied by a partial or complete suppression of urine. It would be difficult to envisage a more dangerous basis for such a surgical operation as cesarean section, a procedure in itself of considerable magnitude and often complicated by further hemorrhage. All judgment should be against it, provided there exists a safer and less radical means of escape."

Cathala states: "Conservative cesarean section is rarely indicated." Alice F. Maxwell declares: "The high maternal mortality following abdominal delivery indicates that surgical measures for the treatment of concealed hemorrhage have been universally unsatisfactory."

The orthodoxy of Irving and Maxwell may be corroborated by an analysis of several tables. The combination of Tables VIII (conservative management) and X (radical treatment) reveal that 2,794 women who were afflicted with some type of ablatio were delivered through the birth canal with 193 deaths—6.9 per cent. If these same women had been cesareanized with the

death rate shown in Table IX (16.8 per cent) there would have been 469 deaths—an increase of 276.

*The Fetus.* The total vaginal births in Table XI amounted to 2,101 with 1,290 deaths—61.4 per cent. If this rate (61.4 per cent) were applied to the women vaginally delivered there would have been 1,715 fetal deaths. If the cesarean rate (70.2 per cent) in the same table be used, 2,061 feti would have perished—an increase of 346. In this hypothetical computation the performance of cesarean section would have sacrificed 276 additional mothers that 346 feti might be exterminated. Cesarean mortalities in placenta previa have already been noted. Here are others which would corroborate the stand of Irving and Maxwell. In 1929, 174 hospitals reported 3,264 cesareans with a mortality of 8.95 per cent in contrast to a puerperal mortality rate of 0.7 per cent for those who were otherwise delivered. *These cesarean deaths constituted 28.0 per cent of all puerperal deaths.* One hundred and twenty-six hospitals reported 2,909 cesarean sections with 292 fetal deaths—a rate of 10 per cent. The death rate of infants (stillbirths and natal) otherwise born was 7.2 per cent. The cesarean deaths constituted 4.5 per cent of all fetal demises. The portent is so ominous that it behooves the obstetric teachers to inculcate conservatism, not only in premature detachments, but in all other directions.

The consensus of opinion is that the operation should be restricted to those cases where these conditions obtain: (1) a fetus near term and alive at the time of operation; (2) a contributory indication such as material pelvic contraction which reasonably would dictate the operation without a detachment (disproportion is infrequent as prematurity is present in about one-third of all cases); (3) a gross anomaly of the soft parts, as strictures, or true cervical rigidity—a relaxation of the cervix is the rule, not an exception; (4) no prior attempts at vaginal interference of any sort; (5) unless the patient is in good condition, with minimal hemorrhage, low



grade of toxemia, and no shock, recuperative measures before the operation, including blood, saline, glucose, Ringer's solution, and general stimulation as required. The question whether a classic or low cervical operation shall be done depends entirely upon the reliance of the operator on his technical skill.

*Hysterectomy.* The removal of the uterus is not an essential detail of the treatment. The policy of such a course when a true Couvelaire uterus is found is based entirely on false premises. Such a uterus rarely bleeds; the infiltration of blood does not spell a dead uterus—if the woman recovers all will be absorbed. The ablation of the uterus only is justifiable when there is an uncontrolled hemorrhage from atony, in the presence of a sepsis, or the danger of it is there from antecedent attempts at delivery.

The danger of cesarean section is graphically portrayed by Irving. Blood transfusions were roughly two and a half to seven times the frequency for sectioned cases as for those vaginally delivered. Toxic apoplexy, in fact all types of ablation, is a fortuitous circumstance which will not recur. It is not right to subject patients to an operation (cesarean) which carries a definite hazard of uterine rupture in subsequent labors, or demand that all later births be sectioned to evade the risk. Neither is it justifiable to sterilize by hysterectomy on specious reasons, thus robbing patients of potential children. Keller states: "Eleven of eighteen women who were observed later became pregnant, and there were sixteen pregnancies with fourteen living children, and no recurrence of uteroplacental apoplexy."

*Manual Dilatation.* The circumstances are so exceptional for the manual dilatation of the cervix, and the conditions must be so characteristically present, that this procedure need no further comment here.

*The Third Stage.* It is usual for the placenta to be expelled with the fetus when the severance is complete. If the placenta is partially detached, the whole serotina being involved, the third stage is completed without difficulty in most instances.

In some cases due to local pathology of the basalis there may be a necessity of using a Credé, and occasionally a manual removal will be necessitated. Every precaution should be taken to conserve blood losses in this period. A small postpartum hemorrhage in a woman already anemic may be disastrous. Every attendant who must assume the care of a woman with a detachment should know the technique of uterovaginal tamponade. It is wiser for the casual operator to tampon too often rather than to neglect it where it might be a necessity.

### CONCLUSIONS

1. The presumptive evidence is nearly conclusive that there are at least four etiologic factors involved in placental separations: traumatic, inflammatory or local degenerative alterations of the serotina, toxemias of varying intensities, and a Couvelaire uteroplacental apoplexy. Real progress in knowledge will come only when these divers types are studied separately. Any attempt to apply a discussion which shall cover the four types indiscriminately merely leads to chaos.

2. The degree of separation of the placenta will be found of less importance than the amount of blood lost. It is notably recognized that uteroplacental apoplexies do not ordinarily have a great excess of bleeding. The toxemia is the serious complication which destroys.

3. Conservative treatment will bring the surest success, vaginal operations second; and cesarean section third. Hysterectomy doubles the mortality of any form of abdominal delivery.

5. The combination of a firm vaginal tamponade with the Spanish windlass apparently promises the greatest chance of a happy termination over all other methods where operative work is deemed essential.

6. As prematurity and fetal death prior to hospitalization play such havoc, everything should center upon saving the mother.

7. All women with placental detachment require a reliable hospital service.

# THE PREVENTION AND TREATMENT OF ECLAMPSIA\*

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THE cause of eclampsia is still unknown, but considerable data indicating a markedly abnormal physiology associated with or perhaps causing the condition have been collected and partially interpreted. The result has been an appreciable reduction in the mortality, due in great part to the treatment which is now directed at improving or correcting the deranged physiology of the various organs and systems involved in the disease. There has also been a constant decrease in the number of patients with eclampsia due to prenatal care.

Our definition of eclampsia is as follows: *clinical*—as the occurrence of convulsions and/or coma in a pregnant or recently delivered woman if associated with hypertension, albuminuria, or edema; *pathologic*—the presence in the liver of periportal hemorrhages and necrosis, of anemic infarcts, or thrombosis of the portal vein or its branches in a pregnant or recently delivered woman if associated before death with any or all of the symptoms or signs previously described.

We believe that the changes in blood and plasma volume are also characteristic of the disease and that the final diagnosis should be based on the clinical course and laboratory findings. The periportal hemorrhages and necrosis which are given as a pathognomonic lesion of eclampsia have been found in a few pregnant patients who had none of the clinical findings of eclampsia. This periportal lesion, however, is peculiar to pregnancy. Furthermore, patients who die ten days or more after the convulsive seizure have normal livers. The most reasonable explanation is that the convulsions and coma can occur in the following types:

1. Eclampsia, characterized by excessive weight gain and/or edema, albuminuria, hypertension, and the various cerebral, visual, gastrointestinal, and renal symptoms and signs.

2. Hypertensive encephalopathy characterized by hypertension, albuminuria, and little or no edema. The so-called "dry eclamptic" probably belongs to this group.

We have studied several patients belonging to the latter group, but the chief difficulty in identifying them is that there is no reason why eclampsia cannot be superimposed on an arterial hypertensive disease. It will require the study of many more cases than we now have to prove this classification beyond question. However, everyone who has studied many cases of eclampsia has noticed differences in response to treatment, especially to sedative drugs. There are many other points of difference, but the lowest maternal mortality for eclampsia is usually achieved by delivery or early fetal death, whereas in hypertensive encephalopathy, delivery is of less importance and the lowest mortality results from the use of large amounts of sedative drugs.

The separation of convulsive toxemia of pregnancy into two types is somewhat academic because our treatment at present is identical. Furthermore, it is difficult during the acute phase of the disease to classify it properly. However, because progress can only be made by attempting to clarify various conditions and diseases, the classification is adhered to.

We have, for a number of years, grouped the various signs and symptoms as follows:

1. *Non-Convulsive Toxemia*: Pre-eclampsia, essential hypertension, vascu-

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lar-renal disease, glomerulonephritis.

- A. Edema (weight), proteinuria, hypertension (individual).
  - B. Cerebral symptoms and signs—headache, dizziness, restlessness, amnesia, increased pulse and respiratory rate and fever.
  - C. Visual symptoms—diplopia, scotoma, decrease in vision, and amaurosis.
  - D. Gastrointestinal disturbances—epigastric pain, vomiting, jaundice.
  - E. Renal disturbances—oliguria, anuria, hematuria.
- II. *Convulsive Toxemia.*
- A. Convulsions—coma.

Non-convulsive toxemia cannot be prevented, but the doctor who practices intelligent prenatal care will appreciate the importance of group A signs and will prevent the onset of the symptoms and signs in groups B to E by the use of diet, proper elimination, and suitable drugs. Likewise, the appearance of any or all the findings in the latter groups indicate that eclampsia is imminent and that more drastic measures must be instituted.

*Edema.* Slight pitting edema of the ankles is a common finding in late pregnancy. It is due in great part to an increased venous pressure, caused by pressure of the uterus on the common iliac veins. Edema of the legs or other parts of the body is abnormal. Marked edema is quite often the first sign of pre-eclampsia and in conjunction with the other signs is found in 40 per cent of the mild pre-eclamptics and in 66 per cent of the severe, in contrast to essential hypertension where the figures are 3 per cent and 14 per cent and in vascular-renal disease where they are 29 per cent and 27 per cent, respectively. Approximately 75 per cent of eclamptic patients have marked edema.

The edema in our patients is not due to a hypoproteinemia. We have been determining serum protein concentrations since 1925 and have a large series from normal

and toxemic patients. Our average serum protein concentration in normal pregnant women is 6.4 Gm. per cent with a standard deviation of 0.4 Gm. per cent; in pre-eclampsia 6.0 Gm. per cent; in vascular-renal groups 6.6 and in eclampsia 6.7 Gm. per cent. Our determination of the colloid osmotic pressure of pregnant and toxemic patients indicates that the osmotic pressure is always above the edema level. The determined and calculated osmotic pressure checks within the experimental limit, indicating that the serum albumin and globulin are normal in their composition. We believe all evidence to date indicates that the edema in most pre-eclamptic and eclamptic patients is due to changes in the permeability of the capillary and cell wall.

*Weight.* Many patients have abnormal gains in weight, which can only be due to retained water, long before they have demonstrable edema. There has been considerable discussion as to the relation between excessive gain in weight during pregnancy and the occurrence of toxemia. Siddall and Mack report that similar excessive or too rapid gains in weight may occur in both normal and toxemic pregnancies. One criticism of their work is that they did not correlate the type of toxemia with the gain in weight. The pre-eclamptic and eclamptic patients usually gain excessively or too rapidly. The average gain in weight in normal pregnancy from various reports is 9 Kg., range 7 to 11. Our normal patients who were followed from twenty-seven weeks to term gained 8.1 with standard deviation of 1.5 Kg., those followed from twenty weeks to term gained 12.4 with a standard deviation of 3.7. If both groups are combined, the average is 9.7 with a standard deviation of 4.3 kilo. Furthermore, during the prenatal period, neither doctor or patient knows what the future gain in weight will be. Therefore for many years, the experienced doctor has calculated the weekly or monthly gain at each examination and been guided in his treatment by this information. The consensus of opinion is that the weight gain of the last

half of pregnancy ranges from 280 to 500 Gm. per week with an average of 400 Gm.

The average weight of the fetus, placenta, and amniotic fluid amounts to 4,200 Gm. and the necessary weight gain due to the physiologic changes of pregnancy (uterus, blood volume, breasts, etc.) amounts to a maximum of 2500 Gm., giving a total of 6.7 Kg. Since 1936 we have been insisting on a weight gain of not to exceed 300 Gm. per week, the total gain not to exceed 8 Kg. One to 3 gr. of thyroid extract in addition to diet has been used since 1937 to aid in preventing excessive gains.

Brown and I have shown that the total weight gain and gain per week are related to the type of toxemia. Twenty-nine per cent of the pre-eclamptics, 14 per cent of the vascular-renal, and 13 per cent of the essential hypertensive patients gained an average of 12 Kg. Seventy-four per cent of the severe pre-eclamptics, 49 per cent of the severe vascular-renal, and 23 per cent of the severe hypertensive group gained at a rate greater than 0.6 Kg. per week. Twenty-four per cent of the severe pre-eclamptic and 10 per cent of the severe vascular-renal patients gained on an average of 1 or more Kg. per week. Single period gains have been as much as 3 Kg. per week and with  $\text{NH}_4\text{Cl}$ , we have noted a 7 Kg. loss in one week. These excessive changes in weight must be due to alteration in the water balance.

*Proteinuria.* The usual qualitative tests reveal no protein in the urine of normal pregnant patients, but a quantitative determination will yield 0 to 0.3 Gm. per twenty-four hours. If a positive quantitative test for protein, which should always suggest toxemia, is found, the patients, since 1935, have been instructed to save the urine in a single container for twenty-four hours, measure it and bring a small specimen to the doctor. Quantitative determinations for protein, chloride and non-protein nitrogen are made. The total excretion of protein per twenty-four hours is usually less than 1.0 Gm. Generally

speaking, as long as the proteinuria was less than 5.0 Gm. per twenty-four hours, the patient was observed at weekly intervals. However, the persistent excretion of more than 5.0 Gm. indicated the need for hospitalization because fetal death in utero due to placental infarction quite often occurred in the arterial hypertensive patient and eclampsia was imminent in the pre-eclamptic. The non-protein nitrogen determination as a measure of the nitrogen metabolism indicated that the protein intake ranged from 1 to 2 Gm. per kilo of body weight. The determination of chlorides was used as a check on the patient's diet. The NaCl excretion must be less than 3 Gm. per twenty-four hours to be of any value as a therapeutic measure in the treatment of edema and as a preventive against further increase in the blood pressure.

Proteinuria (two plus or more) was found on more than two occasions in the urines of 40 per cent of the mild and 88 per cent of the severe pre-eclamptic group; 26 per cent of the mild and 65 per cent of the severe vascular-renal disease group; and 13 per cent of the mild and 50 per cent of the severe essential hypertension group. Albumin forms the greater part of the protein found in the urine. The amount and duration of loss is never sufficient in pre-eclampsia to cause a hypoproteinemia. In severe vascular-renal disease, chronic glomerulonephritis, and nephrosis, the loss is quite often great enough and, especially, the duration of the disease is long enough seriously to lower the serum protein concentration of the blood.

*Urinary Sediment.* The Addis count indicates that the number of casts, erythrocytes, leucocytes, and epithelial cells is slightly increased in normal pregnancy and increased even more in the toxemias. The occurrence of an abnormal urine sediment indicates the need for repeated studies of the patient and a proper diagnosis of the disease. The occurrence for one week or more of red blood cells should suggest acute glomerulonephritis, pyelonephritis, nephro-

lithiasis, tuberculosis, or neoplasm. The presence of casts does not always indicate nephritis. This condition may be present but whenever albumin is present, a proper pH of the urine will result in the precipitation of some of the protein in the tubules, thus producing casts.

*Hypertension.* The normal blood pressure is 90 to 120 systolic and 60 to 80 diastolic. During pregnancy the blood pressure may increase to 121–129/79. A patient who has a systolic pressure of 130 or more on two occasions should be carefully watched. If the pressure is 140 or more, it is definitely abnormal, caused by vascular-renal disease, pre-eclampsia, or glomerulonephritis. An increase in the systolic pressure of 40 or more points, even though the final pressure is less than 140, must be regarded as abnormal.

*Cerebral, Visual, and Gastrointestinal Disturbances.* Headache, dizziness, restlessness, amnesia, increased pulse and respiratory rate, fever, diplopia, scotoma, decrease in vision, amaurosis, and vomiting are all due to cerebral anemia which may be caused by an edema of the brain or by a marked vascular spasm.

Patients differ as to whether cerebral or visual symptoms predominate. We regard the latter as the more serious. The loss of sight may be abrupt and, although the recovery is over a period of days, there is rarely any permanent decrease in visual acuity.

The epigastric pain is a local symptom and may be due to increased intestinal peristalsis or to the subcapsular liver hemorrhage. The jaundice is ascribed to liver impairment and indicates a very grave prognosis. Fever is most likely due to injury of the "heat center" in the medulla, resulting from cerebral anemia or from a possible, but not very probable, "eclamptic toxin."

The occurrence of these symptoms was always associated with hypertension and they were present in 4 per cent of the mild cases of pre-eclampsia, 3 per cent of the mild vascular-renal disease group, 2 per

cent of the essential hypertension group, 50 per cent of the severe cases of pre-eclampsia, 49 per cent of the vascular-renal group, and 37 per cent of the essential hypertension group.

*Renal Disturbances.* The proteinuria, decrease in urine output, anuria, and occasional hematuria are probably due to an edema of the kidney tissue in pre-eclampsia and to arterial spasm and arteriolar sclerosis in the vascular-renal patient. Pre-eclampsia and eclampsia are characterized by an oliguria or even anuria. The urine contains a large amount of protein, but the concentration of salts and non-protein nitrogen is very low.

*Convulsions and Coma.* These are also due to cerebral anemia, resulting from edema in most cases, but also from arteriolar spasm in some cases.

Our treatment of non-convulsive toxemia of pregnancy is as follows:

#### 1. Examination

Ambulatory—weekly or semi-weekly.

Hospital—The patient is weighed and a twenty-four hour urine examination for volume, quantitative protein, and chloride, and three determinations of the blood pressure are made daily.

#### 2. Hypertension

Relaxation—adequate rest at night and 1 hour twice daily. As term is approached, more time may be spent in bed until all time is spent in bed.

Sedation—Phenobarbital (0.03–0.06 Gm. or  $\frac{1}{2}$ –1 gr. three times daily). Potassium bromide (0.6 Gm. or 10 gr. three times daily). Luminal-sodium (0.3 Gm. or 5 gr. one or two times daily) subcutaneously in severe cases.

3. Elimination—Soapsuds enema and mild laxative as needed.

4. Excessive gain in weight—A diet composed of vegetables, fruits, lean meats which must be broiled, boiled, or roasted, eggs and 500

c.c. skimmed or buttermilk. No pie, cake, bread, butter, cream, gravy, soup, or table salt are used.

Pre-eclamptic—Salt-poor, protein 60 Gm., fat 30 Gm., carbohydrate 400 Gm., 2000 calories.

Eclamptic—Fruits and fruit juices with sugar. Limited five to ten days. 1200 calories.

5. Edema—A diet low in sodium and chloride. Watch water balance (weight).  $\text{NH}_4\text{Cl}$  in 1.0 Gm. gelatin capsules is given eight times daily for five days and repeated after a five day interval. If symptoms of cardiac decompensation are present, limit fluid intake to 500–1000 c.c.
6. Oliguria or anuria—Intravenous injection of 500–1000 c.c. of a 20 per cent solution of glucose two or three times daily. Occasionally 500–800 c.c. of a 30 per cent solution are necessary to produce a diuresis. If there is cardiac decompensation, 100–200 c.c. of a 50 per cent solution are used.
7. Proteinuria—Determination of the twenty-four hour amount as a prognostic guide. No specific treatment.
8. Cerebral, visual, and gastrointestinal symptoms—Sedation. Intravenous glucose. Delivery.

Renal function tests are of little value in the pre-eclamptic patients, but are of prognostic value in the other types of toxemia. Ophthalmoscopic examination is of value if pathologic changes are found, but normal findings do not rule out the gravity of the toxemia.

The occurrence of the following symptoms and signs indicate the need for hospitalization of the patient:

*Pre-eclampsia:* Possibility of eclampsia.

Hospitalize: Systolic blood pressure of 170 or more or increase of 40 mm. or more.

Appearance of marked edema, especially of face or abdominal wall (release of bound water).

Abnormal increase in weight with sudden increment of 2 or more pounds per week.

Proteinuria of more than 5.0 Gm. per twenty-four hours or concentration of 0.4 per cent or more (three plus test).

Appearance of cerebral, visual, or gastrointestinal symptoms.

Oliguria or hematuria.

*Essential hypertension and vascular-renal disease:* Eclampsia is uncommon. There is possibility of fetal death, especially after thirty weeks, because of placental infarction, retroplacental hematoma, or abruptio placentae.

Hospitalize: Increase of systolic blood pressure to 200 or more.

Proteinuria of more than 5 Gm. per twenty-four hours.

Marked edema.

Onset of symptoms.

The pregnancy should be terminated if any of the following symptoms or signs persist or increase despite treatment:

1. The systolic blood pressure is constantly 170 or shows a persistent daily increase.
2. The proteinuria always exceeds 5 Gm. per twenty-four hours or the qualitative test is three plus.
3. The weight gain exceeds 100 Gm. per day.
4. Marked edema suddenly occurs.
5. Cerebral, visual, or gastrointestinal symptoms arise.
6. Oliguria, anuria, or hematuria occur.
7. Jaundice develops.
8. The blood N.P.N. is 50 mg. per cent or more.
9. The pulse rate is 120 or more.
10. Edema of the lungs or cyanosis is present.

11. The blood shows an increasing concentration as indicated by an abnormally high or increasing hemoglobin, cell volume,

serum protein concentration or specific gravity.

Our results indicate that the careful medical management of the toxemic patient, if begun early enough, will usually prevent further increase in the severity of the symptoms and signs until the cervix is "ripe." This means that the cervix is effaced, soft and dilatable in the primipara or soft, and partly dilated in the multipara as determined by vaginal examination, and that labor can usually be successfully induced by rupture of the membranes. If contractions have not begun in twelve hours,  $\frac{1}{2}$  to 1 m. doses of pitocin should be given every thirty minutes until the contractions are occurring regularly at three to five minute intervals. The pre-eclamptic patient usually has an oliguria which minute doses of pituitrin exaggerate. Therefore, pitocin is suggested, but it is not completely free of the antidiuretic hormone and should be used with caution.

TABLE I  
F. S. primipara, 19 years old, term 11/11/37

Date	Wt., Kg.	B.P.	Edema	Albuminuria	Remarks
8/5/37	63	135/80	++	0	NH <sub>4</sub> Cl, 8 Gm. daily.
8/10/37	61	130/80	+	0	No salt or fat in the diet.
9/7/37	64	140/90	+	0	Hb. 11 Gm. per cent.
10/12/37	68	170/110	+	0	Complete rest, eclamptic diet, phenobarbital.
10/19/37	67	150/110	+	++	Increasing diet Serum protein 6.4 Gm. per cent.
11/2/37	69	170/120	+	+	Hospital. Ophthalmoscopic exam. normal.
11/3/37		160/100	+++	++	Rupture of membranes.
11/4/37		155/100			Delivery 2,670 Gm. baby.
11/15/37		140/90	0	+	U. C.—75 per cent. U/B—32.
11/18/38	55	110/70	0	0	U. C. 105 per cent. U/B—38.
12/12/39	57	120/80	0	0	U. C. 90 per cent. U/B—36.

The patient who does not respond to treatment or has been neglected is treated by rupture of the membranes and/or the insertion of a bag if the cervical canal is less than 2 cm. long, or, if there is no effacement and dilatation, by cesarean

section under local anesthesia. From 1931 to 1933, 16 per cent of our toxemia patients were delivered by cesarean section with a fetal mortality of 12 per cent for fetuses weighing over 1500 Gm. For 1936 to 1938, 11 per cent were delivered by cesarean section and the fetal mortality was 4 per cent. The incidence of cesarean section in pre-eclamptic patients is 9 per cent and in the vascular-renal 20 per cent. These figures are still too high. The latter high figure is due in great part to a termination usually before term (unripe cervix) and need for tubal ligation.

TABLE II  
S. W.—primipara, 21 years old, term 2/16/37

Date	Wt. Kg.	B.P.	Edema	Albuminuria	Remarks
10/15/36	57	120/80	0	0	Hb. 12 Gm. per cent.
10/31/36	58	140/90	0	0	Ophthalmoscopic exam. normal. No fats in diet.
1/5/37	62	160/110	+	0	Rest one hour twice daily. No salt in diet.
2/2/37	62	180/110	0	0	Complete rest in bed. Eclamptic diet.
2/16/37	62	210/120	0	0	Hospital
2/17/37		170/95	0	0	Rupture of membranes. Pitocin induction.
2/18/37		160/95	0	++	Normal delivery—3,545 Gm. baby.
2/24/37		185/115	0	+++	Urea clearance—85 per cent. U/B 50.
10/26/37		140/95	0		
3/21/38	51	153/95		0	12 wk. preg. Ophthalmoscopic exam. early retinal sclerosis.
4/2/38		130/90		0	Hysterotomy and tubal ligation.
10/10/38		150/90		0	Urea clearance 79 per cent. U/B 30. S.P. 7.5.
10/5/39	53	140/90	0	0	Watch weight.

The case outline for F. S. (Table I) is an example of pre-eclampsia. The abnormally rapid gain in weight, edema, hypertension and albuminuria are typical. The normal hemoglobin and serum protein concentration, normal ophthalmoscopic findings, and low normal urea clearance after delivery and normal one year later are the usual findings. Some of the changes in the signs seem marked but the patient was seen weekly and if any abrupt changes had occurred, she would have been hospitalized at once. We have learned to regard grad-

ually progressive changes with suspicion but not with undue alarm.

The case outline for S. W. (Table II), is an example of essential hypertension. We would classify this case as vascular-renal if the albumin were persistent; if the urea clearance were less than 50 per cent, or if the ophthalmoscopic findings were marked. Note the subnormal weight gain, rapid increase in blood pressure without other symptoms or signs, little or no edema and absence of albuminuria except at delivery. This patient has a normal renal function and with proper care should live for many years. Repeated pregnancies almost always cause further damage and definitely shorten the life expectancy.

Many articles have been written condemning the radical treatment of eclampsia and praising the conservative treatment. Both terms are poorly chosen. Thus a "conservative" treatment which results in maternal deaths is just as extreme as the radical or accouchement forcé which may also result in a maternal death.

The survey by Eden in 1922 illustrates the difference in mortality between mild and severe eclampsia. Any operative procedure which has a high inherent mortality of its own, necessarily increases the mortality of eclampsia. The mortality for severe eclampsia is definitely lowered by early delivery.

MATERNAL MORTALITY  
706 Eclamptic Patients (Eden)

	Mild Per Cent	Severe Per Cent
Natural delivery	5	37
Assisted delivery (forceps)	6	32
Induction of labor	7	26
Cesarean section	11	46
Accouchement forcé	18	63

Hermann reports a close correlation between maternal mortality and the duration of the eclampsia before delivery as measured by the number of fits and by the number of hours before delivery.

MATERNAL MORTALITY 1,633 Eclamptic Patients	
Number of Convulsions	Maternal Mortality Per Cent
1-2	7
3-6	14
7-10	21
11-16	28
17-20	37

MATERNAL MORTALITY 1,379 Eclamptic Patients	
Number of Hours before Delivery	Maternal Mortality Per Cent
0-2	7
3-4	17
5-8	19
9-12	24
13-21	25
over 21	28

Thus there is a very definite time element in the treatment of eclampsia. Waldstein delivered 117 eclamptic patients within three hours of admission and lost two patients, a mortality of 1.7 per cent. Liepmann reports a mortality of 2.5 per cent and Esch of 1.7 per cent, with early delivery. Hermann reports a maternal mortality of 5.3 per cent in 75 patients brought in to the hospital and delivered as soon as possible and a 12.4 per cent in 250 who had a delayed delivery. He treated nineteen patients in the hospital by early delivery with no deaths and forty-one similar cases by late delivery with a 2.4 per cent mortality.

It is obvious that the lowest maternal mortality is obtained in those patients who deliver relatively soon after the onset of the fits. It is also obvious that the eclamptic patient is not a suitable subject for extensive operative procedures and prolonged anesthesia. We believe that the obstetric treatment is the most logical because it is designed to treat the oliguria or anuria, the cerebral anemia and edema (convulsions and coma) and the arteriolar spasm until the patient can be delivered normally. If the cervix is uneffaced and closed and the case a severe one, delivery should be by cesarean section under local anesthesia when the conditions are ideal for the performance of the cesarean section.

Our treatment is as follows:



*General.* Constant observation. Retention catheter. The temperature, pulse and respiratory rate, blood pressure and urine volume should be determined every two hours until the patient is conscious. Oxygen is administered for marked cyanosis.

*Convulsions.* One or preferably more of the following drugs are used: The author

3. Morphine sulfate: 0.016 Gm. ( $\frac{1}{4}$  gr.) every hour until convulsions cease or respirations become 12 per minute.

4. Chloral hydrate: 2 Gm. (30 gr.) in 100 c.c. starch water given by rectum every six to twelve hours.

*Elimination.* Soapsuds enema.

*Hypertension.* Sedation, especially barbiturates and chloral hydrate.

TABLE III

V. R.—Multipara. 33 years old. 30 weeks gestation. No prenatal care

Day	Treatment	Urine c.c.	B.P.	Temperature	Pulse	Hemoglobin Per Cent
1. 11:00 P.M.	Convulsions 1500 c.c. 20 per cent glucose. Coma	Catheter inserted	.	..	136	127
12:00		0				
2. 1:00 A.M.		940	185/130	39	140	
2:00 A.M.		750	160/128	.	128	
3:00 A.M.		300	136/122			
4:00 A.M.		40	140/100	38	128	
5:00 A.M.		15	130/110	38	120	
6:00 A.M.	Awake	45	128/100		120	
7:00 A.M.	1000 c.c. 20 per cent glucose	25	130/110		118	
8:00 A.M.		25			106	
9:00 A.M.	Conscious	540		37	...	90
	Not clear mentally	300	175/140	.		
Total	2500 c.c. 20 per cent glucose	2980				
11:00 A.M.	Bag inserted	60	150/110	37	128	95
1:30 P.M.	Fetus extracted	75	185/145	37	124	
4:00 P.M.	Nasal tube 50 c.c.	....	180/140	37	112	93
4:30 P.M.	1000 c.c. 20 per cent glucose	300				
5:00 P.M.	Karo 100 c.c.	1000	180/130	37	112	
6:00 P.M.	Karo 150 c.c.	450		37	112	
7:00 P.M.	Karo 200 c.c.	....		37	112	
8:00 P.M.	Karo 200 c.c.	50		37	94	
9:00 P.M.	Karo 200 c.c.	75		37	104	
10:00 P.M.	Karo 200 c.c.	450		37	102	
10:30 P.M.	500 c.c. 20 per cent glucose					
11:00 P.M.	Karo 200 c.c.	600	185/130	37	110	
	6 c.c. 50 per cent $MgSO_4$					
3. 1:00 A.M.	Karo 200 c.c.	550		37	110	
48 hr. total	4800 c.c. Rational	5500	185/150	37	96	87

uses #1 and #2 antepartum and adds chloral after delivery.

1. Magnesium sulfate 50 per cent solution: 6 c.c. intramuscularly and 2 c.c. after every convulsion until controlled. Maximal amount is 20 c.c. in twenty-four hours.

2. Luminal-sodium: subcutaneously 0.3 Gm. (5 gr.) every eight to twelve hours.

*Renal and Cerebral Symptoms.* The intravenous injection of from 500 to 1000 c.c. of a 20 per cent glucose solution, two or three times daily given within forty to sixty minutes. Sufficient glucose is injected to insure a urinary volume of at least 30 c.c. per hour. A 30 per cent (500-1000 c.c.) or 50 per cent (200-400 c.c.) solution is used if an adequate output of

urine cannot be produced with the 20 per cent or if symptoms and signs of pulmonary edema appear. Normal saline,

*Diet.* Nothing is given by mouth until the patient is conscious. As soon as the stomach is emptying itself, 50 c.c. of a

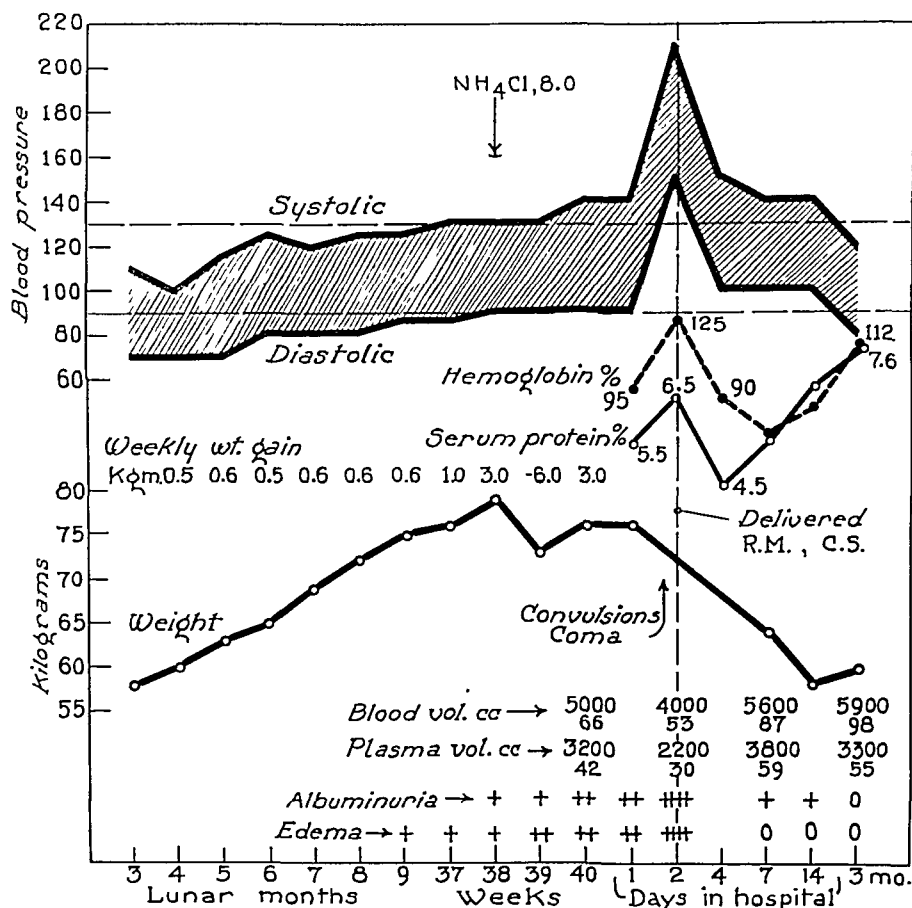


FIG. 1. E. R. Primipara, 20 years old, twin pregnancy. Prenatal care—patient had gained 20 Kg.  $\text{NH}_4\text{Cl}$  was given daily for one week and caused six Kg. loss in weight.

Ringer's, and bicarbonate solutions are contraindicated.

*Pregnancy.* If the patient is in labor, delivery may be hastened by rupture of the membranes or the use of a bag. If the patient is not in labor, we may, after a diuresis has been established, consider:

- Induction of labor, as described above or
- Cesarean section. This operative procedure should only be performed if the case is of the severe type or if cephalopelvic disproportion exists. Local anesthesia should be used and the environment must be suitable.

10 per cent karo syrup solution are injected through a nasal tube and increased 50 c.c. every hour up to the patient's tolerance (usually 200 c.c.) and continued until the patient is conscious and able to take water and fruit juices by mouth.

Data for case V. R. given in Table III illustrate the prompt response to treatment. The patient was thirty weeks pregnant and obviously could not be carried to term. Note the marked diuresis, decrease in temperature to normal, decrease in pulse rate and return to consciousness within ten hours after admission.

Figure 1 illustrates the classical case of pre-eclampsia and eclampsia. Excessive

and rapid gain in weight and then the successive appearance of edema, proteinuria, hypertension, and finally convulsions and coma. The patient's course demonstrates that periodic observations are of no value if the abnormal signs are not properly interpreted and treated. The patient should have been sent into the hospital at the thirty-sixth week. The increased hemo-

of blood and weighed 60 Kg., as compared with a blood volume at term of 5000 c.c. and a weight of 76 Kg. Since the blood volume at term is increased 20 per cent, it should have been 8000 c.c. Note the further decrease in blood volume during the convulsions and coma.

Table IV covers the same patient as Figure 1 and shows the rapid onset of severe eclampsia. Note the oliguria and ultimate anuria, followed by convulsions. Such a patient should be given sedative drugs and hypertonic glucose intravenously to prevent the onset of convulsions. The response to the first injection of glucose was adequate but despite further sedation and another injection of glucose, the patient had more fits, the pulse and respiratory rates and temperature increased markedly, the urinary output was inadequate and the blood (Fig. 1) became more concentrated. Obviously this is a different case from the preceding one and evidently the patient's condition was critical. The severe case is best treated by early delivery, and as the progress of labor was slow, a cesarean section was performed. After delivery the glucose injection produced a marked diuresis, a blood dilution occurred, and clinical improvement was evident.

These two cases illustrate how the response to a systematic treatment can be used to differentiate between mild and severe eclampsia.

#### SUMMARY

The gain in weight per week in normal pregnancy should not exceed 300 Gm. A greater gain should suggest too large an intake of food or an abnormality in the water balance, and a gain greater than 600 Gm. should be regarded as being due to retained water. Appropriate treatment should be instituted early.

A systolic blood pressure of 130 to 139 is considered abnormal and a systolic of 140 or more is indicative of pre-eclampsia, essential hypertension, vascular-renal disease, or glomerulonephritis.

TABLE IV

Day	B P	T	P	R	Urine C c	Treatment	Wt Kg
1 12 hr					200	Intake 1,000	76
2 8 A M	150/110	36	76	18		Rupture of membranes	
12		36	72	20	25	1,500 c c oral	
4 P M	175/120	36	66	20	10	Contractions	
8 P M	210/150	37	112	24	0	Convulsions	
						6 c c 50 per cent MgSO <sub>4</sub>	
						5 gr sod luminal	
						1000 c c 20 per cent glucose	
9 P M	170/130	37	110	28	600	Coma	
10 P M	165/120				300	6 c c MgSO <sub>4</sub>	
12	170/130	38	110	28	140	5 gr sod luminal	
3 2 A M	170/130				50	1000 c c 20 per cent glucose	
3 A M	160/115	39	120	32	150	Coma deeper	
4 A M	150/110				75	Convulsions	
5 A M	150/95	39	132	36	20	Cesarean section	
						Local anesthesia	
						1000 c c 20 per cent glucose	
7 A M	160/115	39	144	32	800	5 gr sod luminal	
8 A M	160/110	38	132	30	425	30 gr chloral hydrate by rectum	
24 hr					2600	Intake 3700	
10 A M	155/110				200	Coma	
12	160/110	37	120	28	150	1000 c c 20 per cent glucose	
2 P M	150/105				550	5 gr sod luminal	64 59
4 P M	155/110	37	110	24	550	Conscious	
8 P M	165/115	37	110		750	1000 c c 20 per cent glucose	
4 1 A M					1500	1000 c c 20 per cent glucose	
8 A M	150/100	37	96	22	1800	30 gr chloral hydrate	
24 Hr					5500	Rational Intake 5800	
5 8 A M	155/110	37	84	18	4500	Intake 3400	
6 8 A M	140/95				5200	Intake 2900	
7 8 A M	140/100				5500	Intake 3000	
14 3 mo	135/75 120/80				2900	Intake 3,500 U C—110 per cent U/B 42	

globin from 95 to 125 per cent, and the rise in serum protein from 5.5 to 6.5 Gm. per cent, indicating a blood concentration, are characteristic of eclampsia. The patient three months after delivery had 5900 c.c.

Proteinuria in pregnancy is abnormal and should always suggest toxemia. A persistent twenty-four hour excretion of 5 Gm. or more warrants interruption of the pregnancy in the interest of both fetus and mother.

The occurrence of toxemia of pregnancy cannot be prevented, but the proper interpretation and treatment of the above signs will usually prevent the onset of the various cerebral, visual, gastrointestinal, and renal symptoms and signs and thus lessen the possibility of eclampsia.

The obstetric treatment of eclampsia yields the lowest mortality. It comprises the control of the convulsions, the promotion of an adequate urinary output, and the securing of a normal temperature, pulse and respiratory rate, a conscious patient, and an early delivery.

## REFERENCES

1. DIECKMANN, W. J. *Am. J. Obst. & Gynec.*, 36: 623, 1938.
2. DIECKMANN, W. J. *Proc. Soc. Exper. Biol. & Med.*, 32: 1127, 1935.
3. DIECKMANN, W. J. *Am. J. Obst. & Gynec.*, 32: 927, 1936.
4. DIECKMANN, W. J. *Am. J. Obst. & Gynec.*, 26: 543, 1933.
5. DIECKMANN, W. J., and BROWN, IRA. *Am. J. Obst. & Gynec.*, 36: 798, 1938.
6. DIECKMANN, W. J., and BROWN, IRA. *Am. J. Obst. & Gynec.*, 37: 762, 1939.
7. DIECKMANN, W. J., and BROWN, IRA. *Am. J. Obst. & Gynec.*, 38: 214, 1939.
8. EDEN, R. *J. Obst. & Gynaec., Brit. Emp.*, 29: 386, 1922.
9. HERMANN, E. *Die Eklampsie*. Berlin, 1929. Urbant Schwarzenberg.
10. SIDDALL, R. S., and MACK, H. C. *Am. J. Obst. & Gynec.*, 26: 244, 1933.
11. SIDDALL, R. S., and MACK, H. C. *Am. J. Obst. & Gynec.*, 36: 380, 1938.
12. ROBINSON, S., and BRUCER, M. *Arch. Int. Med.*, 64: 409, 1939.



# A NEW CLASSIFICATION OF THE TOXEMIAS OF PREGNANCY\*

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**A**DVANCE in our knowledge of the toxemias of pregnancy has undoubtedly been impeded by the lack of a uniform classification of these disorders. Our ignorance as to etiology and the similarity of features of certain of these conditions are among the main reasons for confusion in regard to definition and classification of the toxemias, as is apparent in the literature and published hospital reports. Individual attempts at clarification of the problem and evolution of a standard, workable classification, which all interested would be willing to use, have thus far failed. Some years ago Kellogg wrote: "The conquest of the toxemias of pregnancy depends primarily on a universal acceptance in this country of some index, of some classification, some coöperative mode of study in every great obstetric center."

Realizing the desirability of a uniform classification, the American Committee on Maternal Health, in 1937, appointed a committee consisting of Drs. R. D. Mussey, E. T. Bell, F. S. Kellogg, W. W. Herrick and H. J. Stander to study the problem and, if possible, to reach an agreement upon a simple, workable classification. As the etiology of certain of the toxemias is as yet unsolved and differences of view still exist, it is inevitable that, to accomplish the above-stated purpose, the various members of this committee must be willing to compromise with regard to individual concepts. The fact that the committee has been able to arrive at a mutually satisfactory, tentative classification is indeed gratifying, and it is hoped that maternity hospitals throughout the country will be willing to

adopt the final grouping of the Committee. The Chairman of the Committee, Dr. Mussey, has given the author permission to publish the new classification thus far evolved and agreed upon by all members.

It will serve no useful purpose to discuss here previous classifications, except to indicate how they may be correlated with the following new classification proposed by the Committee:

1. Hypertensive disease
2. Renal disease
3. Pre-eclampsia, severe  
Pre-eclampsia, mild
4. Eclampsia
5. Vomiting of pregnancy
6. Acute yellow atrophy of the liver
7. Unclassified

On April 1, 1939, the above classification was adopted in the New York Lying-in Hospital, and in Table 1 are given the relative incidences of the various types. It will be seen that mild pre-eclampsia accounts for almost 50 per cent of all toxemias. Under this group are included most of the cases which were formerly indexed as "low reserve kidney." The second most frequent type is hypertensive disease, which includes a large percentage of our cases hitherto grouped as "unclassified," as well as some of the low reserve kidney cases. The other types—vomiting, acute yellow atrophy of the liver, eclampsia, severe pre-eclampsia and renal disease, are identical with the earlier classification used in our clinic, except that the term "chronic nephritis" has been replaced by "renal disease." The relative incidence of

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these types thus remains as in our previous studies of the toxemias.

The specific types which need no discussion in this paper since they are similar to, and to a large extent synonymous with, the majority of previously published classifications by various authors, are: vomiting of pregnancy; acute yellow atrophy of the liver; eclampsia; pre-eclampsia, severe; renal disease. For purposes of clarification, however, it should be stated that "pre-eclampsia, severe" includes those cases which in most classifications have been termed "pre-eclampsia," and that "renal disease" is an inclusive term comprising all cases of kidney disease or chronic nephritis of whatever type—chronic glomerulonephritis; arteriosclerotic nephritis (nephrosclerosis); or nephrosis (degenerative type of nephritis). Under "renal disease" should be indexed all patients in whom the past history, present symptomatology and signs, laboratory and chemical findings, such as kidney function, blood chemistry and eye-ground changes, indicate involvement of the kidneys. In "borderline" cases extended observation and clinical and laboratory study may be necessary before a definite diagnosis of kidney involvement or "renal disease" can be established. This, however, is not different from the procedure essential to making the diagnosis of "chronic nephritis" of earlier classifications.

The new terms or designations in the Committee's classification which need some explanation are: pre-eclampsia, mild; and hypertensive disease.

*Mild Pre-Eclampsia.* By mild pre-eclampsia we indicate those patients suffering from a slight rise of blood pressure, some albuminuria and perhaps edema during the latter part of pregnancy; in other words, the findings of pre-eclampsia, but to a limited extent. Shortly after delivery these abnormalities completely disappear and may not reappear in a subsequent pregnancy. In the past this condition has been variously designated. In 1926, Stander and Peckham called this type "low reserve kid-

ney"; it has been labeled "non-convulsive toxemia," "hypertensive toxemia," "hypertension of pregnancy," "albuminuria of pregnancy," "recurrent toxemia," and "kidney of pregnancy." In 1937, Kellogg suggested the term "mild pre-eclampsia."

The following description of this group, taken from Stander and Peckham's paper of 1926, will serve to identify the condition:

"1. An elevated blood pressure which at the end of the puerperium has dropped to a normal level. In most instances this elevation is not very marked, being approximately 150 systolic and 90 diastolic.

"2. The amount of albumin in the urine is never very great, varying before delivery between a fraction of a Gram and 2 Gm. per liter, although the lower figures are most usually observed. The albumin disappears during the puerperium, and the patient leaves the service either with no albumin at all, or with at the most 0.1 Gm. per liter.

"3. The outstanding characteristic is the fact that in subsequent pregnancies, the patient's condition does not become aggravated, and she is as well as, or better than, in the preceding pregnancy.

"4. The blood chemistry, as well as the urine chemistry, reveals nothing abnormal."

*Hypertensive Disease.* Hypertensive disease (hypertensive vascular disease; diffuse arteriolar disease with hypertension; essential and malignant hypertension), just as renal disease, is not a toxemia of pregnancy, but is included in the classification because it is so often first recognized during a pregnancy, is apparently accentuated by gestation, and simulates, in certain features, pre-eclampsia as well as renal disease. Thus it is essential to both proper evaluation and correct diagnosis of the true toxemias of pregnancy, that we include and discuss hypertensive disease, or what has been termed by Keith and his associates, "diffuse arteriolar disease with hypertension."

The syndrome "essential hypertension" has been recognized for many years, and as

the name implies, signifies an elevated blood pressure based upon no apparent associated pathology. Since 1914, when Volhard and Fahr recognized two distinct forms, benign and malignant, essential hypertension has received intensive study both as to its cause and final outcome. The work of Keith, Mussey and their group, Goldblatt and his associates, Pickering, Allen and Adson, Page and Heuer, Nowak and Walker, and of many other investigators, has brought us to a clearer understanding of this condition. In 1932, Goldblatt produced hypertension by constriction of the renal arteries with silver clamps. The subsequent work of the past eight years indicates that this experimentally produced hypertension results from renal ischemia and may be dependent upon humoral influences such as may come from the adrenal cortex and perhaps the kidney itself. Normal blood pressure is maintained by the force of the cardiac contractions, the tonus of the vascular system, the volume and viscosity of the blood and the peripheral resistance. In essential hypertension in man, the cardiac output as well as the volume and physical state of the blood are normal, whereas it is generally agreed that peripheral resistance is increased due to involvement of the arteriolar walls. There is divergence of opinion as to whether human hypertension is of similar origin as experimental hypertension, although some evidence suggests that it also is dependent upon renal ischemia. The peripheral resistance in essential hypertension may be caused by morphologic changes in the arterial vessels, or vasoconstriction of chemical or nervous origin. Experimental evidence has apparently ruled out vasoconstriction of nervous origin. It may well be, as above indicated, that morphologic changes as well as chemical factors play a rôle in the production of essential hypertension. There is little doubt that experimental hypertension, such as that produced by the Goldblatt clamp, is chemical in origin.

In our clinic, Dill and his associates have been investigating experimental hypertension in the pregnant animal and have definitely shown that a clinical syndrome characterized by hypertension, albuminuria, and hematuria, and by pathologic findings of necroses in the kidneys, liver, myocardium and placenta results from renal ischemia produced during the pregnancy, although no obvious effect seems to accompany or result from pregnancy in an animal previously rendered hypertensive.

Hypertensive disease may antedate pregnancy or may first appear during gestation. It is conceivable that pregnancy is a predisposing factor in the production of arteriolar changes resulting in hypertension, which may become permanent in the form of an "essential hypertension." Certainly pregnancy is accompanied by vascular changes, such as spasm of the arterioles, which may conceivably play a rôle in the production of hypertension.

The characteristic finding in this condition is an elevated blood pressure without any signs or symptoms indicative of renal involvement. The past history, the first appearance and course of the hypertension, the evaluation of other signs or symptoms, the laboratory findings as they relate to kidney function and the examination of the eyegrounds are the main factors in establishing a correct diagnosis. It is essential to rule out renal disease, after which it becomes necessary to determine the extent of the arterial disease. To this end, examination of the eyegrounds is all important.

In the benign form of hypertensive disease, the blood pressure is usually not elevated to extreme degrees, no albuminuria exists, ophthalmologic examination reveals only minimal changes in the vessels and symptoms are commonly absent. In the severe forms, or malignant type, the retinal vessels show more marked involvement, and finally kidney function becomes impaired. It is thus clear that from the benign form, there is a transition to the malignant type where the condition sooner or later shows renal involvement.

Keith and his group have divided hypertensive disease or what they prefer to call "diffuse arteriolar disease with hypertension," into four groups, the first being the well recognized benign essential hypertension; the second including those with more marked hypertension, slight symptomatology and no retinitis; the third, those with mild vasospastic retinitis; and the fourth, the malignant hypertension. The retinal changes proceed from minimal involvement to angiospastic retinitis, to edema of the discs with spastic and organic narrowing of the arterioles with diffuse retinitis.

## DISCUSSION

It is not the purpose of this paper to discuss prognosis and treatment in the various groups or types of toxemia, but merely to outline the new classification. That this classification is simple and work-

TABLE I  
INCIDENCE OF TOXEMIA—NEW CLASSIFICATION  
108 Cases in 1,503 Pregnancies  
(April 1, 1939—September 30, 1939)

Type of Toxemia	No. of Cases	Percentage of Total
Vomiting of pregnancy	7	6.5
Acute yellow atrophy of liver	1	0.9
Eclampsia	4	3.7
Severe pre-eclampsia	7	6.5
Mild pre-eclampsia	51	47.2
Hypertensive disease	31	28.7
Renal disease	7	6.5
Total	108	100.0

able is shown by the fact that we have employed it during the past nine months without undue difficulty in the transfer from our previous to the present classification. To a certain extent we have been able to correlate the statistics of the previous seven years with this new classification, as is shown in the accompanying tables, and particularly in that representing our ma-

ternal mortality figures for the whole period.

From Table I it will be noted that the total incidence of toxemias, including renal and hypertensive disease, is slightly over 7 per cent. Mild pre-eclampsia and hypertensive disease together account for about three-fourths of the whole series. Renal disease, severe pre-eclampsia and vomiting of pregnancy are of equal frequency and of about the incidence reported in our earlier studies, where these types were designated as chronic nephritis, pre-eclampsia and vomiting of pregnancy, respectively. We

TABLE II  
MATERNAL MORTALITY IN THE TOXEMIAS OF PREGNANCY

Type of Toxemia	Maternal Deaths	
	No. of Cases	Percentage Incidence in 2,276 Toxemias
Vomiting	0	0
Pre-eclampsia, mild (low reserve kidney)	0	0
Pre-eclampsia, severe	0	0
Eclampsia	1	0.044
Renal disease (chronic nephritis)	0	0
Hypertensive disease (unclassified)	0	0
Acute yellow atrophy	3	0.132
Total	4	0.176

Total toxemia mortality:

4 maternal deaths in 2,276 pregnancies, or 1.76 per 1000 pregnancies

have had an unusually high incidence of acute yellow atrophy of the liver, as shown in Tables I and III. In Table II are recorded the maternal mortality rates in the 2,276 cases of toxemia, treated in the New York Lying-in Hospital during the period September 1, 1932 to December 31, 1939, while in Table III are given all maternal deaths occurring in our service during the same period. From these tables it will be noted that the toxemias of pregnancy accounted for 7.1 per cent of our total uncorrected maternal mortality in 30,457 patients dis-



charged from the hospital. The toxemic deaths occurred in acute yellow atrophy of the liver and in eclampsia. During the seven year period we had eight cases of acute yellow atrophy with three deaths, or a mortality of 37.5 per cent; while during

## SUMMARY

The number of cases of toxemia of pregnancy recorded in this paper is too small to allow definite conclusions. However, the analysis of this series indicates that the new classification of the Com-

TABLE III

## MATERNAL MORTALITY FOR PERIOD

September 1, 1932—December 31, 1939

Pavilion, Private and Berwind (Outdoor) Services

During this period there were 56 deaths in 30,457 discharged patients, a maternal mortality rate of 0.184 per cent, or 1.84 per 1000 patients discharged, or 2.06 per 1000 pregnancies. The causes of death in these fifty-six patients are shown in the table.

Cause of Death	1932	1933	1934	1935	1936	1937	1938	1939	Total	Per Cent of Total
Infections:										
Antepartum and postpartum.....	..	1	1	3	4	1	..	1		
Postabortal.....	..	..	..	..	1	..	1	..	13	23.2
Pneumonia:										
Antepartum and postpartum.....	2	1	..	2	..	1	..	..	6	10.7
Postpartum hemorrhage:										
Vaginal delivery.....	1	..	..	1	..	1	1			
Following section.....	..	..	1							
Ruptured uterus.....	..	1	..	..	..	..	..	..	6	10.7
Cardiac disease:										
Cardiac failure.....	..	1	..	1	1	..	1			
Postpartum hemorrhage.....	..	..	..	..	..	1	..	..	5	8.9
Pulmonary embolus.....	1	..	2	1	..	..	1	..	5	8.9
Toxemia:										
Acute yellow atrophy.....	..	1	..	..	1	..	..	1		
Eclampsia.....	..	..	..	..	..	1	..	..	4	7.1
Premature separation of placenta.....	..	..	1	..	1	1	..	..	3	5.3
Pyelonephritis.....	..	1	..	1	..	..	..	..	2	3.6
Circulatory collapse:										
Pituitrin intravenously.....	..	..	..	1						
Surgical shock.....	..	..	..	..	..	1	..	..	2	3.6
Cerebrovascular accident.....	..	..	..	1	1	..	..	..	2	3.6
Anesthesia.....	..	1	..	..	..	..	..	..	1	1.8
Postoperative hemorrhage.....	..	..	1	..	..	..	..	..	1	1.8
Tuberculosis, miliary.....	..	..	..	1	..	..	..	..	1	1.8
Placenta previa, antepartum.....	..	..	..	1	..	..	..	..	1	1.8
Chorionepithelioma (postpartum).....	..	..	..	..	1	..	..	..	1	1.8
Blood dyscrasia-erythroblastic splenomegaly.....	..	..	..	..	1	..	..	..	1	1.8
Suicide.....	..	..	..	1	..	..	..	..	1	1.8
Not determined—insufficient data.....	..	..	..	..	..	1	..	..	1	1.8
Total.....	4	7	6	14	11	8	4	2	56	100.0

the same period we had forty-seven cases of eclampsia with one maternal death, or a mortality rate of 2.1 per cent. It may be of interest to state that the fatal cases of acute yellow atrophy of the liver showed the typical clinical picture as well as the pathologic lesions in the liver at autopsy.

mittee appointed by the American Committee on Maternal Welfare, can readily be applied, being simple and workable. Although the author has been an advocate of certain different concepts, he is more than willing to use this classification in the indexing and study of the material in the

New York Lying-in Hospital, and hopes that all maternity services throughout the country will adopt this new classification. Should this obtain, we would be in a far better position to gain valuable information regarding the etiology and treatment of these disorders of pregnancy. Cooperative

studies, similar to those already being conducted by the cooperative clinical group interested in syphilis complicating pregnancy, are most desirable, but, of course, cannot be successfully carried out unless all clinics entering into such a study employ a uniform classification.



MORTALITY among the offspring of toxemic mothers is appreciably higher than among those without toxemia. . . . A large proportion of the deaths is probably due to procedures instituted because of the toxemia rather than to the disease itself.

From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

# NUTRITION IN PREGNANCY

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OF prime importance in maternity care is the nutrition of the expectant mother. She must be regarded in a class apart, with many special needs to be considered. In these days of altered economic conditions there is an added difficulty of adjusting the family food budget to provide the adequate and essential food items for the pregnant and nursing mothers. The deficiencies of the diet of the non-pregnant woman become dangerous when maternity intervenes. It has been shown by many surveys that the diets of adults show deficiencies in various items ranging from 40 to 90 per cent, and in prenatal groups the deficiencies in essential items may range from 12 to 50 per cent.

Nutrition requirements are usually stated under four headings: a minimum or maintenance level; a level adequate for health, a 50 per cent increase over the minimum; an optimum nutrition level; and curative levels. In pregnancy we should at least hope for an "adequate for health" level. Such a diet should provide protective, energy giving and regulatory constituents. It should have the ingredients so balanced that no drain is placed on body tissue; it should provide for growth of the woman's body as pregnancy advances; and while supplying the fetus with material for growth, still be sufficient to put aside a reserve for the work of labor and for the onset of lactation.

What should a proper diet for a pregnant woman contain and how may we educate and help her to obtain it? It is not enough to advise her to drink plenty of water, eat vegetables and go lightly on starches and meat. Such advice is worse than none. It is necessary to be specific and yet use terms which are understandable by the average

citizen. That 1 Gm. of calcium per day is essential, is Greek to a clinic patient, but that she should drink a quart of milk a day is common sign language. Yet, if we do not understand the Greek ourselves we cannot translate our knowledge into the sign language of milk, meat, grains, and greens.

The average weight gain during pregnancy amounts from 20 to 25 pounds. Dieckmann<sup>1</sup> recommends limiting the weight gain to the equivalent weight of the fetus, placenta, amniotic fluid, and the maternal physiologic changes incidental to pregnancy. In other words about 16½ pounds (7.5 Kg.) or an average weekly gain of ½ pound after the end of the negative phase of pregnancy.

A controversial point in regard to weight gain during pregnancy and the birth weight of the child still exists. Rucker<sup>2</sup> feels that a carefully calculated diet, low in fluid, fat and carbohydrate, high in protein, and with a total of 1800 calories has definitely reduced the weight of babies, shortened the length of labor and caused a minimum of premature babies compared with a control group. Unless such a diet provides the essential food constituents it may do harm, and the parasitic action of the fetus will be at the expense of the maternal organism.

The energy requirements or heat units or calories of a pregnant woman's diet vary with her weight and with her activities. If we accept as a standard 30 calories for every 2.2 pounds, we should add 75 calories for each hour of active moderate work. Thus, the average woman (120 to 150 pounds) would need from 2000 to 2500 calories, while the nursing mother would need a decided increase, from 20 to 40 per cent. Calories, or heat units, are derived from three principal ingredients of the diet:

protein, fat and carbohydrates. These are the building and energy giving sources of our diet.

Protein is required in proportion of 1 Gm. or 15 gr. for every Kg., or 2.2 pounds of body weight. Proteins are derived from two sources: animal and vegetable. The proteins break down in the body to form elemental units, called amino acids. These units serve to build and repair the body tissues, promote growth of the fetus and to keep the nitrogen balance level. The animal proteins, derived from animal tissues, meat, milk, eggs, cheese, form or should form, half of protein requirements. The remainder will come from the vegetables: peas, beans, and other sources. A high protein diet in the expectant mother is believed to raise the prothrombin and fibrinogen content of the maternal blood, and so protect against hemorrhage.

Certain proteins such as lactalbumin of milk, beef protein, ovalbumin of eggs and glutinin of wheat, contain all the essential amino acids and the average diet should contain all these articles to prevent a qualitative deficiency. The reserve or deposit protein in the adult human body amounts to approximately 2 Kg. or 5 pounds. During the latter five months of pregnancy approximately 500 Gm. of nitrogen is stored up as a reserve for labor and lactation. The protein requirement for the fetus has been given as 60 Gm. of nitrogen, for the placenta 17 Gm., the amniotic fluid 1 Gm., the mammary glands 17 Gm. and for the uterine enlargement as 39 Gm.

From a table of food values it is simple to ascertain the approximate protein sufficiency of a diet. Thus one serving each of milk, eggs and roast beef with three servings of bread would contain 1100 calories and yield 54 Gm. of protein, four-fifths of the protein requirements of the average woman. Over 70 per cent of this is protein of high biological value.<sup>3</sup>

Vegetable proteins are animal protein savers, but they are inadequate sources of amino acids and should only be used as an

accessory source of protein supply. McCarrison<sup>4</sup> feels that 66 per cent animal protein in the diet, recommended by the Nutrition Committee of the League of Nations,<sup>5</sup> is an unnecessarily high figure. He recalls the high biological value of the vegetable group of proteins. Many unemployed and low paid families are unable to purchase even a minimal animal protein maintenance ration.

Deficiency in protein in pregnancy may lead to nutritional edema and tend to anemia, poor muscular tone, lowered resistance to disease, and poor milk supply. Restriction of protein lowers the nitrogen level and leads to nutritional edema due to utilization of the body tissues for the normal protein requirements.

The two groups of energy supplying foods are carbohydrates and fats. Fat is not only a concentrated source of energy, but is of primary importance as a carrier of essential vitamins, and may be essential to their proper utilization. From observation of women who choose their own diets, it seems that fat intake is fairly steady throughout pregnancy. The observed intakes vary from 103 to 139 Gm., and these values are well above those suggested by the Royal Society Food (War) Committee<sup>6</sup> of 100 Gm. per man. Deficiencies in fats may lead to diminished fertility. Excessive fat ingestion has been suggested as a cause of eclampsia. Butter may be regarded as the best fat.

The number of calories or heat energy units required in a diet, after the adequate requirements of protein have been met, are made up in part of fat which represents 25 to 30 per cent. The remaining calories are derived from carbohydrates, 50 to 60 per cent, which are essential in the diet only as a source of energy, supply for food for the growing fetus, and to spare the proteins from being burnt up by the higher metabolic rate of pregnancy. Their intake must be carefully controlled, for an excess of carbohydrates leads to a diminished intake of proteins and vitamins. Excesses in

carbohydrates lead to an unhealthy gain in weight.

One of the most frequent forms of carbohydrate used in excess in the diet of pregnant women is white bread, which is cheap and bulky. There has been insufficient insistence on the total substitution of whole grain bread for white bread. The highly milled flours and cereals are deprived in the milling of important nutritive elements, such as the vitamin B complex, vitamin E, unidentified blood making factors and the proteins of the germ and bran. A slice of whole wheat bread not only has the same caloric value as a slice of white flour bread but it possesses a greater value in calcium, phosphorus, iron and vitamin B. Carbohydrates in the diet may easily be lowered by shifting to 5 per cent or 10 per cent vegetables from those with a higher carbohydrate content.

Various mineral constituents of the diet are essential for the nutrition of the expectant mother. We may discuss the three most important: calcium, phosphorus and iron.

*Calcium.* The estimated intake of calcium should approximate 1 Gm. per day in the first four months of pregnancy and then be stepped up to 1.5 Gm. in the last five months. This increase is due to the observation that a pregnant woman begins to store calcium and build up a reserve after the fourth month, at which time the fetal demands begin; the fetus begins a storage of its own after the seventh month. A full term fetus contains an average of 24 Gm. of calcium.

The basic source of calcium in the diet of a pregnant woman should consist in a daily quart of milk, which contains 1.15 Gm. of calcium. Skim milk contains just as much calcium as whole milk and may be used if the fat of the cream is not desired in the caloric requirements. The remaining calcium needs should be supplied in other dairy products. If milk is not palatable, an attempt may be made to supply the whole requirement by commercial preparations of calcium. The difference in cost is apparent.

Every organ in the body is influenced by or has an influence upon the calcium metabolism. The utilization of calcium in the body depends upon a proper supply of sunshine or vitamin D. Even with a very high calcium and phosphorus intake, these minerals will not be utilized without an adequate dosage of vitamin D.

A deficiency in the calcium intake leads to many abnormal states. The mother suffers from cramps in the legs, headaches, insomnia. A deficiency may be the cause of dental caries. Eclampsia has also been alleged to be due to a deficiency of calcium. In the fetus of the first pregnancy of a mother whose diet is deficient in calcium, no signs of the deficiency are noted, for the fetus is parasitic, and will drain its necessary lime salts from the host. In rapidly succeeding calcium deficiency pregnancies, however, the fetus is said to suffer from osteoporosis, rickets, and poor tooth formation.

*Phosphorus* is widely distributed in an average diet containing milk, eggs, meat, fish, cheese, and poultry, and generally little lack is seen. Its mobilization again depends upon vitamin D, and a proper ratio, 1 to 1.5, must be maintained with calcium in the blood.

*Iron.* It has been calculated that a pregnant woman requires 20 mg. of iron daily. A total storage of 900 mg. of iron is required during pregnancy, for the human fetus at term contains 400 mg., while 500 mg. of iron is required for the placenta. Women in the reproductive cycle, subject to the recurring blood loss of the menstrual flow have high iron requirements. The need of iron is increased in both pregnancy and the nursing period. The increased fluid content of the blood in pregnancy leads to a diminution of the hemoglobin which has been termed, "the physiologic anemia of pregnancy." In many instances secondary anemia is present, and, rarely, a pernicious type is found. It is common to find hemoglobin reading in pregnancy below 70 per cent. Many women need an iron intake greater than can be attained in their diets,

and commercial preparations should be administered, especially in the last trimester of the pregnancy.

Iron is found in beef, liver, egg yolk, oysters, some pitted fruits and in leafy vegetables. It is surprising to note that one-half cup of cooked mustard greens contain as much iron as a generous serving of corned beef or six oysters, and one serving of liver a week will greatly supplement the iron content of other foods. The addition of wheat germ to the diet adds a considerable amount of iron as well as increasing the storage of available iron from other sources. This is but another argument for the use of coarsely ground wheat cereals and flours. The deficient diets of the poorer classes often show clearly in the anemic, pasty-faced, weary and dreary looking pregnant women of our clinics, the lack of available iron supply.

*Iodine.* A deficiency of iodine affects both reproduction and lactation. For this reason fish or sea foods should be ordered at least once a week in the diet of a pregnant woman. In goiter belts iodized salt should be used in the diet as a prophylactic against disorders of the thyroid gland.

*Salt (Sodium Chloride).* Both the sodium and the chlorine ion in table salt when used in excess have been blamed as causes of toxemia of pregnancy. Excessive use of salt leads to a retention of water in the tissues. Consequently, a reduction in salt intake and the sodium ion toward the end of pregnancy or where kidney insufficiency is suspected, is in order.

*Water.* This regulative factor of the diet is generally required in the proportion of 1 Gm. or c.c. for each caloric value of food intake. Intake of 2 liters (2 quarts or eight glasses, large size) would be required to supplement the average diet. The fluid content of various foods lowers the amount of water to be drunk.

Generally speaking the amount of water required is that sufficient to promote a proper dilution of minerals in the blood. An output of 3 pints of urine daily is objective evidence of an ample fluid intake.

When edema arises in pregnancy, nephritis must be looked for, nutritional edema ruled out and a water balance must be established, intake being measured to approximate the output, changing the amount daily as required. That 10 pounds of fluid may accumulate in the body tissues before clinical edema becomes evident is of importance in a consideration of weight changes during pregnancy (Bierlein).

"Most estimates of requirement for vitamins today are based on determinations of the minimum amount necessary to prevent visible and recognized symptoms of deficiency, plus a factor of safety to cover individual variations. The size of the factor of safety varies with the viewpoint of the estimator. Such estimates when applied in dietary surveys supply a means for detecting gross deficiency but they do not tell adequacy, if we mean by the latter term amounts necessary to provide optimum needs, optimum health." Strauss<sup>7</sup> states: "I feel that it is wise to hold out for high levels, particularly in view of the many metabolic and gastrointestinal changes which occur in pregnancy and which probably alter the absorption, utilization and requirement of nutritional factors."

There is increasing evidence that mild and frequently unrecognized deficiencies of some vitamins are prevalent in this country. They are due to such factors as inadequate diet (economic), unbalanced diets (ignorance or idiosyncrasies); loss of vitamins (cooking) and ignorance regarding extra requirements.

*Vitamin A* is fat soluble. It is found in halibut and cod liver oil, butter, milk, cream, and egg yolk, green and pigmented vegetables. The daily requirement in the diet of a pregnant woman has been variously calculated as from 5000 to 9000 International Units. Presence of this vitamin promotes growth and has been said to prevent infection and has much to do with promoting the reproductive process. Qualitative dark adaptation time tests readily show deficiencies. Some skin conditions of pregnancy have been found amenable to

increased intakes of vitamin A and calcium. Since this vitamin is soluble in mineral oil, it has been recommended to avoid such laxatives at meal times.

*Vitamin B<sub>1</sub>* is soluble in water and is easily destroyed in cooking as it is susceptible to heat. It is found in whole grain cereal, brewer's yeast, meat and vegetables. It is essential in pregnancy since it aids digestion, stimulates the appetite, has a protective function for the nervous system and stimulates lactation.

Minor degrees of B<sub>1</sub> deficiency are seen in the marked nausea and vomiting cases of early pregnancy. Extreme deficiencies are reflected in the polyneuritis and paralysis present in pernicious vomiting cases. Lack of a certain fraction of the B<sub>2</sub> group of vitamin leads in tropical countries to a pernicious type of anemia. In India one-third of maternal deaths are due to this disease. Daily requirements of vitamin B<sub>1</sub> are estimated at 300 to 1200 International Units. Expressed in terms of thiamin chloride, 1 to 1.4 mg.

*Vitamin C* is found in raw vegetables and the citrus fruits. It is essential for its effect upon the dental apparatus and bones. Its ingestion is said to promote good tooth and bone formation, to prevent bone lesions, to prevent scurvy, and is concerned with the cellular nutrition of the pulp peridental membranes. Indeed, modern dental nutritional studies suggest that vitamin c from the standpoint of the mother, is of almost as great importance as calcium. The sore gums or acid mouth of many pregnant women is a manifestation of a deficiency of this vitamin, and immediate relief is seen when four to six whole oranges are eaten each day. The old saying, "a tooth for a child" is probably due as much to a lack of vitamin c as to a lack of calcium in the diet. It has been recommended that in the daily diet of pregnancy 1500 International Units of this vitamin or 75 of ascorbic acid be included. This is roughly equivalent to the ascorbic acid (or vitamin c) content of three medium sized oranges.

The ascorbic acid intake is closely reflected in the blood serum content of this dietary factor. The fetus draws like a parasite on the vitamin c supply of the maternal host, the umbilical cord blood containing from two to four times the amount of ascorbic acid present in the maternal blood.<sup>8</sup> This suggests that an oversupply is required by the nursing mother, particularly one who has a premature baby. A deficiency in the vitamin c content of the maternal diet is also said to lead to a latent scurvy in the fetus, and to a predisposition to brain hemorrhages in labor.

*Vitamin D* is essential for proper utilization of calcium and phosphorus. Like vitamin A, it is fat soluble, and is found in fish liver oils, milk, and egg yolk. In addition to mobilizing calcium and phosphorus, it aids in preventing fetal rickets. It is possible that grave deficiencies leading to calcium metabolism disturbances may lead to the production of postpartum hemorrhage. A deficiency may tend to occasion prematurity of labor. It is the current impression that this vitamin should be administered to all pregnant women, summer or winter. It is interesting to note that far larger amounts of vitamin D are used in animal husbandry for cattle, swine, and poultry than are employed for human consumption. As yet, no basic requirements of vitamin D for the pregnant woman have been worked out, and recommendations vary from 300 to 800 units.

*Vitamin G* is one of the subdivisions of the vitamin B complex group. If B<sub>1</sub> is supplied in sufficient amounts little worry need be had over the other fractions in the diet. Nicotinic acid and riboflavin may be prescribed for appropriate clinical deficiencies.

*Vitamin E*, the fertility vitamin, is present in such sources as wheat germ oil and lettuce. It may be added to the diet in abnormal cases, as habitual abortion or repeated premature labors, or in the occasional patient, pregnant after a long sterile period, where it appears necessary to

supplement the natural reproductive forces and functions.

### SUMMARY AND CONCLUSIONS

The nutritional factors in pregnancy vary with the weight and activity of the particular individual, and must be increased as pregnancy advances.<sup>9</sup> For an average woman of 125 to 150 pounds, active in her domestic life, from 2000 to 3000 calories may be indicated. This value should be derived from a diet containing from 60 to 100 Gm. of protein, 70 to 100 Gm. of fat, 150 to 400 Gm. of carbohydrates. The mineral requirements should range from 0.7 to 1.5 Gm. of calcium, 1.0 to 1.5 Gm. of phosphorus, 20 mg. of iron. The vitamin requirements are: from 4000

### Breakfast

Orange  
Oatmeal with whole milk  
Toast and butter  
One cup of coffee, tea, or a glass of whole milk

### Dinner

Pot roast of beef or other lean meat  
String beans or carrots or both  
Baked potato, bread and butter  
Glass of whole milk  
Baked custard

### Supper or Luncheon

Baked rice and cheese  
Apple and celery salad  
Whole wheat muffins and butter  
Stewed apricots  
One cup of cocoa made with whole milk, or a glass of whole milk  
A glass of whole milk may be taken before bedtime.

An analysis of this diet shows that it contains the following values:

Protein	Fat	Carbo- hydrate	Calo- ries	Calcium	Phos- phorus	Iron	Vitamins in Sher- man Units					Excess	
							A	B	C	D	G	Acid	Base
65.35 Gm.	70.55 Gm.	250.25 Gm.	1966	1.446 Gm.	1.695 Gm.	14.10 mg.	9803	401	129	24	427	28.6	49.0

to 8000 International Units of vitamin B, or, expressed as thiamin chloride, 0.3 to 1 mg.; from 400 to 2000 International Units of vitamin C, or, expressed as ascorbic acid, 20 to 100 mg.; and 300 to 800 U.S.P. units of vitamin D.

Murphy and Bowes<sup>10</sup> have suggested as basic foods for the diet during pregnancy the use daily of:

- 1 quart milk
- 2 to 3 servings of leafy vegetables
- 2 to 3 servings of other vegetables
- 3 to 4 servings of fruit (1 or 2 servings of citrus fruit)
- 3 or more slices of bread, whole grain varieties preferred
- Meat or fish as recommended by physician
- 1 egg
- 1 to 2 ounces of butter
- Cod liver oil or vitamin A, B, D and concentrates, as directed by physician.

The following sample day's diet issued by the Children's Bureau of the United States Department of Labor furnishes a working basis on which modifications may be planned.

It will be noted that this diet approximates the average optimal requirements for pregnancy.

While the iron value is slightly below the average stated requirements it could easily be made up by an additional beef or calf liver ration twice a week. The deficiency in vitamin D is indicative of the need for its supplementary administration in the diets of many women, particularly in the northern part of the United States in the cloudier seasons of the year.

### SUMMARY

In summary it may be said that not until recently has the nutritional aspect of maternity care received the attention it deserves. Only two standard textbooks carry anything but a cursory mention of the subject.<sup>11,12</sup>

The possible relation of dietary factors to such problems of pregnancy as toxemia and prematurity are beginning to be recognized and investigated.



The health and well being of the pregnant woman and her unborn fetus demand an enlarging interest in the question of nutrition.

#### REFERENCES

1. DIECKMANN, W. J., and SWANSON, W. W. Dietary requirements in pregnancy. *Am. J. Obst. & Gynec.*, 38: 523, 1939.
2. RUCKER, M. P. Effect of diet on outcome of pregnancy. *Kentucky M. J.*, 35: 329, 1937.
3. MOE, R. J. Nutrition in pregnancy. *Minnesota Med.*, 21: 779, 1938.
4. McCARRISON, R. Nutritional needs in pregnancy. *Brit. M. J.*, 2: 256, 1937.
5. Nutrition Committee of the League of Nations, Technical Commission of the Health Committee, Report on Physiological Bases of Nutrition, II. B. 4, 1936.
6. Royal Society Food Commission, London. Food War Committee, 1919. Harrison and Sons.
7. STRAUSS, M. B. Personal communication.
8. TEEL, H. M., BURKE, B. S., and DRAPER, R. Vitamin c in human pregnancy and lactation. 1. Studies during pregnancy. *Am. J. Dis. Child.*, 56: 1004, 1938.
9. GARRY, R. C., and STIVEN, D. Review of recent work on dietary requirements in pregnancy and lactation, with an attempt to assess human requirements. *Nutrition Abst. & Rev.*, 5: 855, 1935-1936.
10. MURPHY, D. P., and BOWES, A. DeP. Food habits of mothers and congenitally malformed children. *Am. J. Obst. & Gynec.*, 37: 460, 1939.
11. BECK, A. C. *Obstetrical Practice*, 2nd Ed., Baltimore, 1939. Williams & Wilkins.
12. ADAIR, F. L. *Obstetrics and Gynecology*. Philadelphia, 1940. Lea & Febiger.



It must constantly be remembered that merely because a woman suffering from toxemia gives birth to a dead fetus, this is no proof that such condition was responsible for its death, and other causes should be sought as diligently as if toxemia were absent.

From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

# NATURAL LABOR

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NATURAL labor is the ideal objective for the termination of every pregnancy. In order to accomplish this it is absolutely necessary that the patient have the benefit of intelligent obstetric management, not only during labor, but throughout the duration of the pregnancy and the puerperium. A very large proportion of all labors will proceed to a natural termination, if permitted. Errors of commission are much more common in obstetric practice than errors of omission. The recognition at the earliest possible time of abnormal conditions may do much to secure a normal labor or minimize the dangers that are to be anticipated.

In reviewing protocols of fatal obstetric results several facts are outstanding. First, a labor which would have been natural has been converted into an unnatural labor by unwise and unnecessary interference on the part of the attendant; second, failure to recognize abnormal conditions early enough to anticipate bad results and conduct the case in such a manner that the best results could be secured under the conditions present, or in some instances to change an abnormal labor into a natural labor; third, unwise selection of the procedure best suited to the pathologic conditions present; fourth, although the proper operative procedure may have been chosen, it is done at the wrong time.

The practice of obstetrics is coming quite definitely under the influence of this fast age and the old dictum that "to do good one must do no harm" seems to have been forgotten. The attendant has no moral right to do anything which will even to the slightest degree increase the hazard to his patient. It is a fact that any interference, however simple, during the progress of labor is potentially harmful and the

reasons for doing anything must greatly outweigh the disadvantages of doing nothing. The experienced obstetrician too frequently finds himself confronted with the necessity of steering between Scylla and Charybdis with danger to the mother on one hand and to the baby on the other. Many procedures have been proposed to accomplish some doubtful purpose, which in themselves definitely increase the dangers to the mother and the baby. The purpose of the doctor should be to keep out of trouble; all too often the death of the baby or the mother is directly due to over-active interference with the normal process of labor.

There is a definite tendency in the literature toward more active obstetrics, the value of which is very doubtful, notably outlet forceps operation, routine version and extractions, routine breech extraction, induction of labor in every case at term, and particularly rupture of the bag of waters for the induction of labor or to hasten the progress of the first stage. Some of these procedures when done by their proponents in strict accordance with the proposed indications and conditions may yield satisfactory results. However, the influence of this teaching on the less expert members of the medical profession tends toward more active interference with labor, which results in unwise application of these methods, very often with disastrous results. The continued practice of this teaching can only effect a tendency away from natural labor.

## INDUCTION OF LABOR

The exact cause of the onset of labor is not known, but it is well recognized that the nearer a pregnancy is to the time that labor would start spontaneously the easier

it is to induce the onset of labor. Our methods, however, for determining how close a patient is to the termination of her pregnancy are crude and uncertain. Furthermore, there is at the present time no satisfactory method for the induction of labor. That most widely used is quinine and castor oil and, as generally applied, this will induce labor in exact proportion to the proximity of the pregnancy to term. But quinine has been charged with the death of infants in patients sensitive to the drug. A few cases have also been reported in which quinine is believed to have contributed to the rupture of the uterus. Its use has been abandoned in some clinics.

The use of quinine, castor oil, pituitrin and the Voorhees bag is not without danger. Their application is never indicated except when the reasons for the induction of labor are important enough to outweigh the objections to their use. The induction of labor by any method for the convenience of either the doctor or the patient cannot be too strongly condemned.

When an attempt is made to induce labor, the doctor will usually begin with the less radical methods. If these attempts fail, it becomes a matter of pride to succeed in his undertaking and he proceeds with each method more radical than the preceding one, burning all his bridges behind him. After days of uncertainty, the case terminates with a dead baby and an exhausted mother. To assume the responsibility for a possible outcome such as this, one needs a real reason for the undertaking.

It is inconceivable from a biologic standpoint that the bag of waters is of no value in the mechanism of labor. No one will deny that the bag of waters offers a protection to the baby in an actively contracting uterus. There is a variable limit to the length of time a baby can survive after rupture of the bag has occurred. It may be impossible for the fetus to be safely delivered before this time has passed. Prolonged labor from inefficient uterine action

can never be prognosticated with certainty. The outcome not only for the baby, but for the mother as well, in this difficult complication of labor will often be determined by the length of time the bag of waters remains intact. In a large clinic with a proportionate number of prolonged labors, the importance of an intact bag of waters is frequently observed. Although the so-called "dry labor" frequently terminates as a natural labor, there is a certain definite number of cases in which rupture of the bag of waters plays a major rôle in the death of the baby. The promiscuous and routine procedure of rupturing the bag of waters for the purpose of inducing labor or shortening the first stage of labor is a very questionable practice and will in a certain definite proportion of cases convert natural labor into an abnormal labor.

#### BREECH

The practice of "breaking up" the breech as a routine procedure is gaining in popularity in various clinics throughout the country. This is an example of the trend of obstetric teaching away from natural labor. The hazard to the baby is inherently greater in breech presentation than in cephalic presentation. A large number of breech cases will deliver spontaneously to the umbilicus, so that this presentation may be classed with natural labor.

Although long series of cases have been reported in which the mortality in breech extractions has been lower than in spontaneous delivery of the breech, it must be remembered that these cases were handled in a hospital under supervision of expert obstetricians. These results are not comparable with those to be expected in the hands of the general practitioner who is not under supervision and who delivers only two to four breech cases a year, and who, because of his limited experience, cannot be expected to carry out an often complicated procedure with success. In a series of 16,000 consecutive deliveries at Cook County Hospital, there were 604 spontaneous breech deliveries with a corrected

mortality of 3.8 per cent. There were thirty breech extractions with a mortality of 16 per cent. It is believed that the conservative attitude in respect to breech presentation, which allows a natural labor to remain natural as long as possible, is responsible for this low mortality.

#### ROUTINE VERSION AND EXTRACTION

Not many years ago a furor for the performance of routine version and extraction swept the medical profession throughout this country. Fortunately, the enthusiasm was short-lived because of the devastating results for mother and baby. This procedure is perhaps the most noticeable example of the crude efforts to improve upon the expert performance of nature. Version and extraction, to be reasonably safe, must be done with a most accurate compliance with the conditions laid down in every textbook, and for reasons sufficient to justify the performance of an operation which in itself carries a high mortality and morbidity.

#### ROUTINE FORCEPS DELIVERIES

For a great many years, obstetricians have shortened the second stage of labor by an outlet forceps operation. This was contrary to the old teaching which advocated the use of forceps only when necessary. In recent years this method has been given the stamp of approval by an increasing number of teachers of obstetrics, until at the present time in many hospitals it is almost a routine procedure.

It has been stated on good authority that the incidence of cerebral hemorrhage is lower in cases which are delivered by means of outlet forceps and episiotomy than when the head is allowed to deliver spontaneously. From a mechanical standpoint it is difficult to understand how a head dragged by forceps through a vagina enlarged by an episiotomy will receive less traumatism than a head forced through the same opening by the powers of labor. The success of so many outlet forceps operations is an indication of the amount

of insult a child's head can survive rather than a credit to the art of obstetrics.

Outlet forceps delivery performed with the conditions actually present, namely, perineum beginning to bulge, complete anterior rotation, and episiotomy, is in itself the least objectionable of all the procedures which have been discussed. However, the routine application of this method, which frequently requires that a patient making normal progress toward a natural delivery be put to sleep and delivered with forceps, differs only in degree from the method that under the same circumstances pushes the head up out of the pelvis to do a version and extraction. It must be remembered that many errors are made in the diagnosis of the degree of descent of the head in the pelvis, and many doctors fail to distinguish the difference in forceps operations with respect to the amount of descent and degree of rotation. Therefore, if routine outlet forceps delivery is generally taught, there will be a tendency to extend the application of the forceps to cases above the outlet with a still greater increase in maternal and fetal injury.

#### THE THIRD STAGE OF LABOR

The third stage of labor perhaps offers more opportunity and temptation to interfere with natural labor than does any other stage. Although the student is taught with all force possible that the "hands off" policy with intelligent management will result in the least loss of blood and the fewest complications in this stage, when he is left to himself, he will yield to the temptation to manipulate and massage the uterus in a usually futile attempt to hasten the delivery of the placenta. Every sin of commission that can be imagined is commonly practiced to hasten the progress of the third stage. To the human mind the third stage seems to be incompatible with noninterference.

The objective in the third stage is to secure a spontaneous delivery of the

placenta with a complete and untorn maternal surface and with the smallest blood loss. To attain this objective it is imperative for the attendant to await patiently the process of natural labor until the placenta is separated, whereupon it will be delivered spontaneously, or may be expelled by simple and harmless assistance. Manipulating the uterus, early attempts at Crede expression, before placental separation, positively interfere with this mechanism and are not only unnecessary but cause complications which result in bleeding and delay the delivery of the placenta.

#### CONCLUSIONS

During the last two decades the death rate in the first year of life has been markedly reduced. This reduction has occurred almost entirely after the neonatal period. With the recent increased attention given to prenatal care, there has been some small decrease in the number of deaths from conditions which can be influenced by better management during pregnancy. As the study of this question continues the light of investigation is being focused more and more upon the delivery room. Further improvement in infant mortality must be accomplished by reducing the hazards to mother and infant during labor. Since natural labor involves the least risk, it is obvious that nothing should

be done that will change a labor that could be natural into an abnormal labor.

It is true that a relatively small number of pregnancies and labors will be abnormal and require intervention of one kind or another. These pathologic cases, however few in number, require skill and judgment beyond those usually acquired by a doctor whose obstetric practice constitutes only the smaller amount of his work. In a hundred obstetric cases, ninety-five are of such a nature that the experience gained in their management is of little or no value to the doctor when he is confronted with a major complication of obstetrics. The answer to this problem presents numerous difficulties. Perhaps one could visualize a plan whereby in every community in the United States two or three physicians, especially trained in obstetrics, would be available for the aid of the general practitioner in managing this small percentage of his routine labor cases.

The practice of obstetrics seems to have been subjected to more criticism from the outside than any other branch of medical practice. There is no doubt that further improvement in the practice of obstetrics can and will be accomplished. But it is to be hoped that any faults will be recognized and problems solved by the medical profession rather than by outside agencies, to the end that childbirth will be made even more safe in the United States.



# FACTORS INFLUENCING THE SAFETY OF PAIN RELIEF IN LABOR\*

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**O**PINION regarding pain relief in labor is in a chaotic state. Medical literature relating to obstetrics and to anesthesia contains endless controversial discussions regarding which combinations of agents and which methods of pain relief are most satisfactory. Obstetricians are being criticized because of the high incidence of operative deliveries, high fetal mortality rate, excessive maternal morbidity and mortality, and, more recently, because of the occurrence of permanent damage to the nervous system of the newborn child. All these circumstances are looked upon by some critics as sequelae of efforts at complete relief of pain. A glaring omission in the literature is the failure to emphasize the necessity for intelligent supervision of the physiologic activity of mother and child. In other words, it has apparently been assumed that administration of adequate quantities of pain relieving drugs to mothers in labor, constitutes the necessary extent of service.

In what follows, we wish to emphasize the necessity for careful physiologic management of mother and child during whatever periods of drug depression are thought justifiable. In other words, we hope to make clear the necessity of a competent anesthetist as a member of the obstetric team whenever an attempt is made to eliminate completely the pain of labor. The need for careful supervision of the mother and child progresses as the ideal of painlessness is approached. A large group of drugs, constantly growing larger, is utilized to promote comfort in childbirth. All are administered with the hope of producing sleep, amnesia, analgesia or anesthesia.

The agents available, whether administered by injection, by inhalation, or through the alimentary tract, all produce undesirable and sometimes unrecognized side effects detrimental to the welfare of both mother and child.

## DRUG EFFECTS OTHER THAN PAIN RELIEF

*Disturbance of Reflexes.* The autonomic nervous system is easily thrown out of balance by drugs which relieve pain. Either obtundation or hyperactivity of reflexes may be the result. No physician can prophesy whether reflex disturbances will take place in a given patient from a particular drug and dosage. If the reflex mechanism of labor itself is abolished or made hyperactive, it is a problem easily dealt with by the obstetrician. If, however, the pharyngeal and laryngeal reflexes are obtunded, a foreign body may obstruct respiration. If at the same time the vomiting reflex is hyperactive, a condition presents which must be cared for at once if permanent damage to the unborn child or even the mother is to be prevented. Depression of cough reflex promotes the chance of later chronic obstructive phenomena while reflex vocal cord adduction may result in acute oxygen want, dangerous or even fatal to the fetus. Depression of ciliary activity of the respiratory tract is now a recognized effect of the pain relieving drugs. How such action may affect the newborn is yet to be determined.

*Muscle Relaxation.* Loss of muscular tone of the mother during labor may, of course, decrease the effectiveness of expulsive effort. More important to the welfare

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of the baby, however, is the possible interference with respiratory exchange due to relaxation of tongue and pharyngeal mus-

SOD. PENTOBARBITAL gr.  $4\frac{1}{2}$  ORAL.

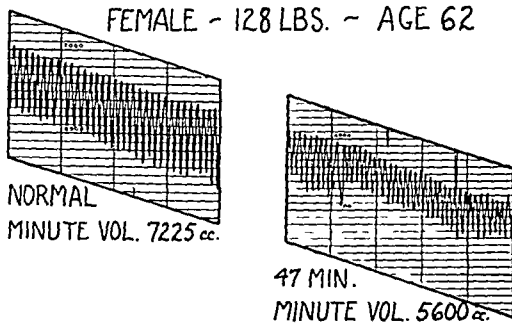


FIG. 1. Effect of oral administration of  $4\frac{1}{2}$  gr. (290 mg.) sodium pentobarbital upon respiratory exchange. Similar records made before and after administration of other nonvolatile agents show, with only two exceptions, similar reduction in respiratory efficiency, the reduction increasing with increased dosage and the susceptibility of the patient. Scopolamine hydrobromide and paraldehyde have little or no tendency to decrease respiratory exchange.

cles and the resulting encroachment upon the air spaces. Such respiratory obstruction is particularly apt to occur late in the second stage when more profound drug dosage is necessary, and when the result may be a poorly oxygenated respiratory center with its attendant failure to maintain function at birth. Even the most experienced anesthetist finds it difficult to recognize, by observation alone, respiratory obstruction of a degree quite capable of causing signs of oxygen want in the fetus.

**Psychic Depression.** Loss of conscious coöperation of the mother handicaps obstetric procedure in making aseptic technique difficult and in depriving the obstetrician of voluntary aid in expulsion. Less frequently is it appreciated that a woman with absent or fogged mental faculties may fail to turn her head, change her position or otherwise safely supervise her condition when vomiting or other threat to safety occurs.

**Depression of Respiratory Center of Mother and Baby.** Opiates, barbiturates and other nonvolatile drugs, as well as inhalation agents in sufficient dosage, all cause de-

pression of the respiratory center of mother and child. Rarely can doses of nonvolatile agents adequate for pain relief be administered without measurable decrease in minute volume pulmonary ventilation. (Fig. 1.) A most potent depressant of cell activity is oxygen want. At the moment of delivery, the child's respiratory center is usually subject to at least some depression from drug action and from trauma. If at the same time, blood low in oxygen bathes the respiratory center, depression is further enhanced.

**Technical Faults.** Untoward results following improper management of the period of drug depression are, of course, largely dependent upon the four extraneous pharmacologic characteristics considered above. Nevertheless, further consideration of the technical difficulties of maintaining normal physiology may not be amiss. The ease with which vomitus may be aspirated is not generally appreciated. If the circumstance is recognized at once and properly treated, little harm may result. A minor degree of respiratory obstruction may be difficult or impossible for the inexperienced physician to recognize or to relieve. The degree of interference with gaseous exchange from obstruction of the air passages becomes comparatively more important as the total minute volume is less due to the presence of central respiratory depression. The need for prompt and sure relief of obstruction and restoration of oxygen is imperative. (Fig. 2.) During the administration of inhalation agents of slight potency, such as nitrous oxide, the temptation to permit mothers to inhale oxygen-deficient atmospheres is always present. Even during periods of milder drug effects, such as those accompanying administration of moderate doses of nonvolatile agents during the first stage, the safety of mothers and particularly of children can best be assured by the attention of well trained and experienced physicians who have mastered the art as well as the science of pain relief.

The presence of fetal movements in utero, the fetal heart rate and the presence

or absence of meconium in the outlet discharges are the three criteria at present available by which we may judge the condi-

tioned administration of inhalation agents while the head is passing the outlet.

Marked change in fetal heart rate has

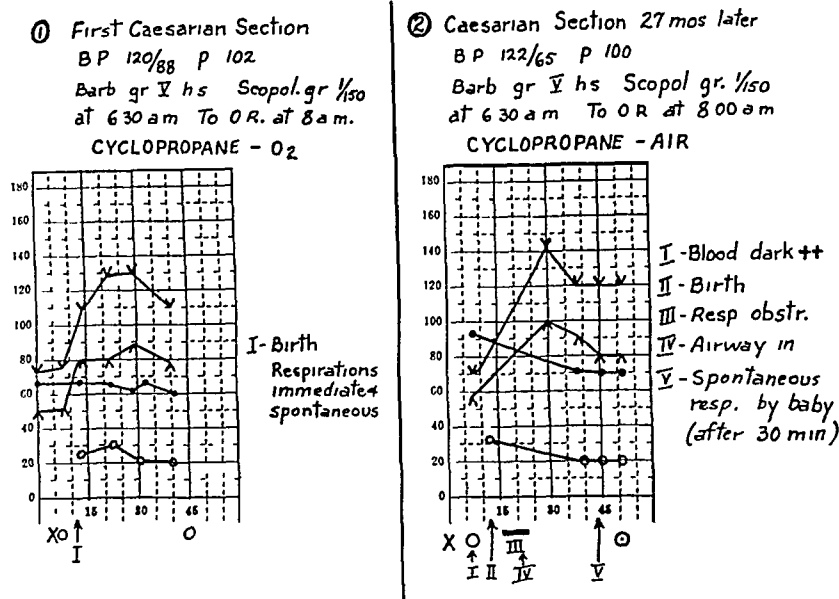


FIG. 2. Records of two cesarean sections performed upon the same mother. Condition of mother the day before and medication on both occasions were similar. (Code: V—V = blood pressures; ●—● = mother's pulse rate; ○—○ = mother's respiratory rate.) Intense fear was present when the woman came to the operating room on each occasion and was the apparent cause of low blood pressure and small pulse pressure on each occasion. In the first instance, cyclopropane was administered with excess oxygen and a smooth induction occurred, with restoration of mother's normal circulatory condition as soon as she was anesthetized. The baby cried spontaneously. In the second instance, cyclopropane in an atmosphere without excess oxygen was used. Induction was rough with severe respiratory obstruction. Mother's blood was cyanotic when incision was made. Restoration of a free airway, good oxygenation and probably of normal maternal blood pressure relations was not accomplished until eight minutes after the cord had been severed. Strenuous efforts were necessary over a period of a half hour before the baby's respiration was established.

tion of the unborn child. Since the pulse rate is particularly sensitive to oxygen deficiency, a means whereby it may be under constant observation during the second stage of labor is important. The delay involved in reporting by word of mouth from an observer to the anesthetist during the second stage has been found unsatisfactory and unsafe. The equipment shown in the illustration (Fig. 3) has been found satisfactory in putting the anesthetist in possession of essential knowledge for: (1) controlling the oxygen content of the mother's inspired atmosphere so as to avoid fetal anoxemia; (2) directing the expulsive efforts of the mother; and (3) well

long been among the criteria indicating rapid delivery. Such change may, of course, be neurologic in origin. It may also be due to an uncontrollable circulatory defect. Not infrequently, however, both in the first and second stage of labor have we been able by well timed and adequate administration of oxygen rich atmosphere to the mother, to restore the fetal heart rate to normal and eliminate the need for forced delivery. An example of such control is illustrated in the accompanying chart. (Fig. 4.)

#### DISCUSSION

It is obvious from the foregoing that agents which relieve pain have certain



secondary effects always tending toward interference with efficient respiratory exchange in the mother. The system of trans-

elimination of carbon dioxide is no less intricate. Any respiratory or circulatory defect in the mother, any physical embar-

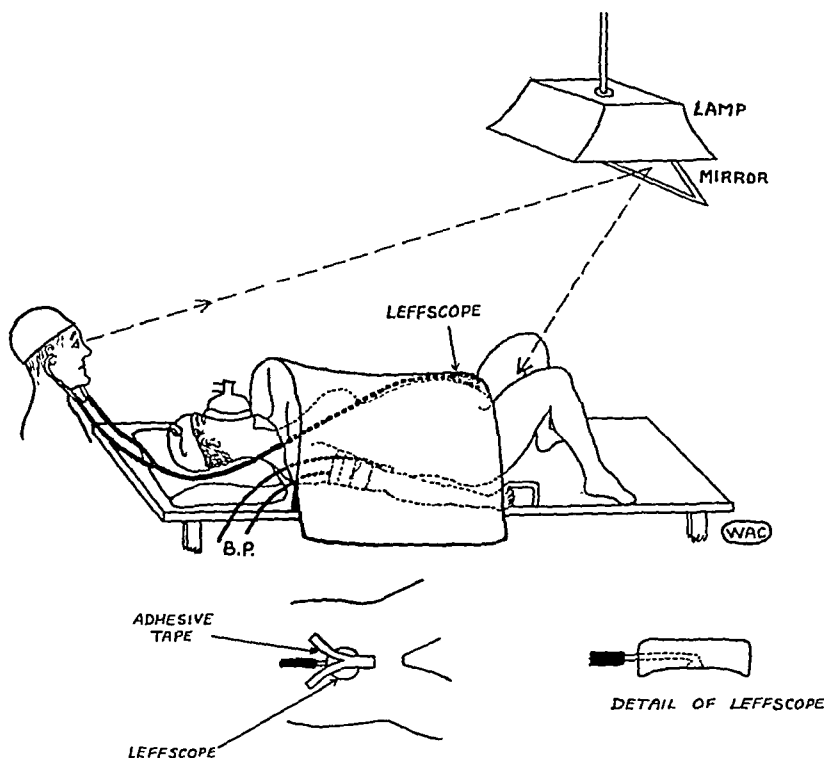


FIG. 3. Equipment to put the anesthetist in command of the necessary information to guide him in proper management of the physiologic condition of mother and child during second stage: Stethoscope bell is heavy metal (diameter 7.5 cm., weight 930 Gm.), no diaphragm, boilable, and has given satisfactory auscultation of fetal heart sounds during several years' use (Leff, *M. Am. J. Obst. & Gynec.*, 20: 108, 1930). Stethoscope and cuff on arm for observation of maternal blood pressures. A mirror attached to lamp frame by adjustable ball and socket joint makes perineum visible to anesthetist throughout expulsion.

Concentration of anesthetic gas or vapor can be varied to suit the needs of various individual types of contractions. Evidence of when to increase concentration is gained from three sources: the mother's impression, the anesthetist's hand palpating the abdominal wall, and from the mirror.

Marked changes in fetal heart rate can often be rectified by judicious enrichment with oxygen of the atmosphere inhaled by the mother. Excess oxygen, if properly timed, need not interfere with proper pain relief even when nitrous oxide is the sole agent in use. If the anesthetist palpates the abdominal wall and observes through the mirror late in the second stage, he can assist the obstetrician by encouraging or restraining the mother's voluntary effort according to the obstetrician's desires. Transmission of information by word of mouth from the obstetrician or his assistant to the anesthetist is too slow to permit the sudden changes in activity which are essential.

port by which oxygen is conveyed from the atmosphere breathed by the mother through her alveoli, blood vessels and heart, to the placenta and thence through the fetal circulatory system to fetal tissue cells is a complicated one indeed. The

rassment to the cord, even the physical changes incident to uterine contraction, all these are potent sources of embarrassment to this transport system. The full extent of the influence of these extraneous characteristics of pain relieving drugs upon

the initiation and maintenance of respiration of the child after birth, is not yet completely understood.

be conversant with the pharmacology of pain relieving drugs, their administration and the technical means of counteracting

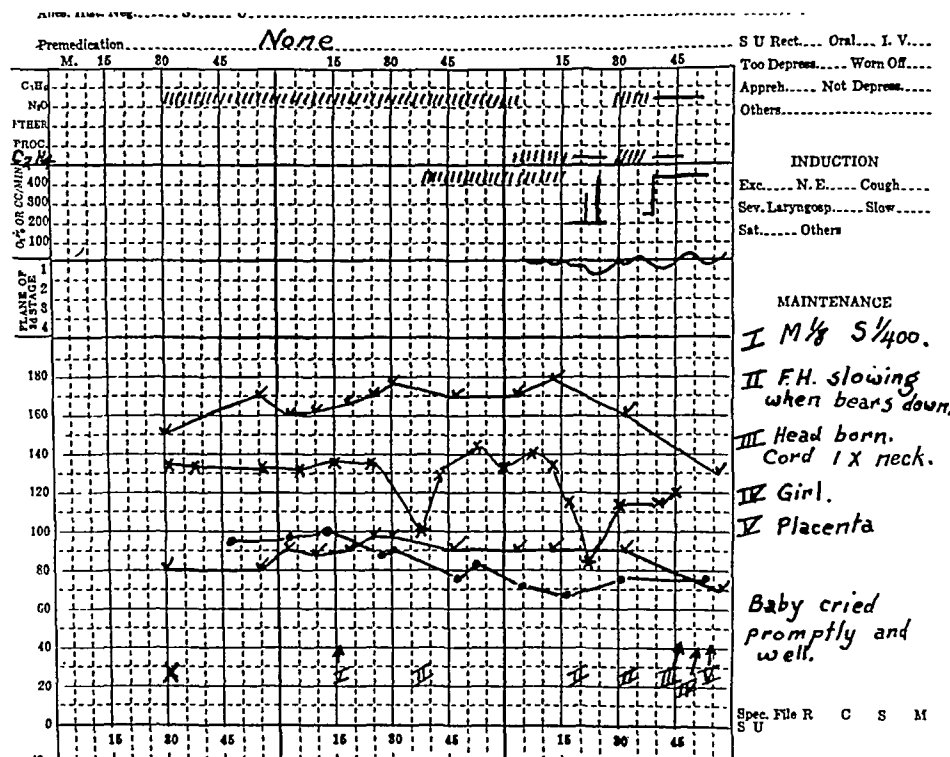


FIG. 4. Record of pain relief during second stage accomplished by inhalation of nitrous oxide-oxygen and ethylene-oxygen. (Code: V—V = systolic and diastolic blood pressures of mother; ●—● = pulse rate of mother; X—X = pulse rate of fetus.) Many observations of fetal heart rate were made that were not recorded. The tendency is seen in the record, however, for the pulse to decrease in rate on certain occasions. The anesthetist observed that the maximum decrease in pulse rate occurred during and following the height of uterine contraction, when simultaneous lower concentration of oxygen was being inhaled. Administration of pure oxygen as soon as the uterus relaxed after each contraction was capable of presenting the decrease in fetal heart rate. The baby was born spontaneously over an hour later and cried immediately. Not infrequently have we seen similar evidence of oxygen want in the fetus (decreased heart rate) during the first stage, relieved by administration to the mother, between contractions, of oxygen-rich atmosphere or pure oxygen gas.

It is well recognized that, even when no drugs are administered to the mother, transit through the birth canal is a hazardous journey. Interference with oxygen and carbon dioxide transport is recognized as not the least of the dangers. It is our belief based on clinical experience that if complete pain relief in labor is to be our aim, a physician thoroughly conversant with the physiologic mechanism of gas transport and methods of aiding and correcting it, should be a constant member of the obstetric team. If the pain of labor is to be safely and completely abolished, such a physician should

their undesirable side effects. The surgical profession has accepted the fallacy of the belief that the surgeon can spread his attention to cover pain relief for his patient, supervise the welfare of the patient and yet offer the best that he has of surgical skill. In obstetrics, two patients are concerned. The transport system for oxygen and carbon dioxide is more complicated. If we are to aim at safe and efficient pain relief in obstetrics, we must admit the anesthetist to the obstetric team. To fulfill his function, such an individual must recognize wherein the problem of pain

relief in obstetrics differs from the similar problem in surgery. Observation and supervision of the condition of the fetus in utero and its mother is perhaps more difficult than is similar service for the surgical patient, at least it is different. Few surgical anesthetists have devoted sufficient attention to the obstetric problem to perfect themselves in it.

In one American city a well trained anesthetist has for several years specialized in obstetric anesthesia. This plan has proved satisfactory to him both economically and professionally as well as to several obstetricians and their patients. His work is confined largely to one lying-in hospital. In coöperation with the obstetricians, he supervises dosage of nonvolatile agents during the first stage of labor. He is responsible for observation and care of mother and fetus while they are affected by drugs. These duties are sandwiched between administration of volatile or gaseous agents during second and third stages of labor; thus he is available at all times to recognize at once disturbed physiology in mother and fetus or newborn and to rectify or treat promptly physiologic disturbances. Such a plan may be found a future solution of many of the obstetrician's difficulties.

#### CONCLUSIONS

In America in recent years we have indulged too much in the hope for a possible drug or combination of drugs which may be expected to abolish safely all pain in connection with childbirth. We have looked upon new and untried drugs as the solution of our difficulties when we might better have devoted our efforts to a search for better ways of using agents with which we are already, at least partly, familiar. We have neglected to a large extent consideration of disturbances of physiologic balance in mother and child which are and always

will be necessary accompaniments of administration of all drugs which relieve pain.

The authors believe that if complete safety and complete pain relief are to be our aims, we must admit that the two objects *tend* to be reciprocally incompatible—more safety, less pain relief; more pain relief, less safety. We believe our aim ought to be the most complete abolition of pain compatible with perfect safety to mother and child during labor and thereafter. If such is the aim of obstetric practice in America, pain relief must wait upon safety. If practical considerations for the present preclude the services of a physician well trained in both the science and the art of pain relief, drug administration must be limited, and pain relief must be limited, to an extent compatible with the knowledge, skill, and experience of the physician in charge. The doctor must appreciate that the more familiar he is with the effects of drugs which he uses, the more likely will he be to treat properly disturbances which result from drug effects. Taking up the use of a new drug or combination of drugs because some one else reports success with it is a dangerous experiment to be undertaken with care. The safeguards efficacious with one method are often futile with another.

We would admonish the practitioner not to forget that ether, chloroform or nitrous oxide combined with appropriate mental suggestion, have in the past in the hands of those skilled and experienced in their use, offered great satisfaction and safety to many mothers and children. The same may be said of opiates and scopolamine. The skill, knowledge, experience and attention of the physician, devoted to the dosage of a particular drug or combination of drugs, and methods of correcting promptly all ill effects, shall be the gauge by which is determined the extent of pain relief legitimately to be sought for in a given case.



# VERSION AND BREECH DELIVERY\*

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## DEFINITIONS

**V**ERSION means turning. Obstetrically it means changing the part of the fetal ovoid which presents at the pelvic inlet. It is named respectively for that end of the ovoid which presents at the completion of the maneuver. Thus it is cephalic if the head end of the fetus is caused to present, podalic if the buttocks and/or lower extremities are caused to present. Only the latter will be discussed here.

The turning is in itself a complete maneuver; it does *not* include the extraction of the baby after it is accomplished. While in most cases extraction is an immediately sequential procedure, it need not, and in some cases *must* not, be so carried out.

We shall have no reference herein to so-called "elective podalic version."

There are several varieties of podalic version, named respectively in reference to the technique employed. That referred to herein is the "combined" variety accomplished by simultaneous manipulation within the uterus, and outside the abdomen.

## INDICATIONS

Since, as will be seen, it is never desirable to have the podalic end of the fetus present, podalic version is done only for some direct objective more urgent than the general desirability of the more favorable cephalic presentation.

*Chief among such indications are:* faults of presentation, as many cases of transverse presentation; some impacted face or brow presentations; some compound presentations; occasionally, as in twins, normal cephalic presentation, where conditions for the operation are easy and expedition of delivery is legitimately indicated.

Formerly almost the only resource in such situations, version has been superseded in many cases by cesarean section. It should today be reserved for those cases in which the fulfillment of proper indications for its employment permits its use with nominal risk. It is used here primarily in the mother's interest. Therefore, it should not be selected when it represents greater risk to her than the dilemma from which extrication is sought.

In prolapse of the cord, the operation may be employed, primarily in the interest of the fetus. But it is generally without avail in that interest unless the labor may thereby be *quickly* terminated. Only where its conditions are ideal, may it be used to finish labor rapidly without great risk to the mother. In any other situation, therefore, in which the cord prolapses and cannot be replaced, and the labor cannot be managed deliberately, it is better to accept the loss of the baby rather than to subject the mother to great risk of danger in performing version.

Version still has a distinct place in the treatment of placenta previa, though here

\* From the Margaret Hague Maternity Hospital.

also the hydrostatic bag and cesarean section have partly supplanted it. It is especially when used for this condition that immediate extraction is dangerous and contraindicated.

While general conditions of the mother not infrequently make desirable the rapid termination of labor, it is relatively very rare that version will constitute the procedure of choice to accomplish it.

The employment of version in cases of impaction of the head in the inlet by relative cephalopelvic disproportion is debatable. It was formerly importantly depended on in such situations, even in high degree of disproportion. And there is no doubt, as a matter of experience, that it has many times successfully solved such difficulties. But since it is inevitable that in many such cases ideal conditions for its employment will not obtain, recognition of the danger to both mother and child has tended to lessen its use. Cesarean section will properly supplant it in some cases. Expectancy and forceps will, in our opinion and experience, supplant it in nearly all the others.

There are two principal techniques used in version. That of Braxton-Hicks is done by restricting the intra-uterine manipulation to the introduction of two fingers through the imperfectly dilated os cervicis, bringing down one limb only, and desisting after this is accomplished. The prolapsed half breech acts as a tampon against, and dilator of, the lower uterine segment. It is a difficult procedure, is applicable *only* to certain cases of placenta previa, and is today rarely used, having been supplanted by other methods.

The second technique involves the introduction of the whole of the internal hand into the uterus. Conditions for this procedure are, ideally, that there shall not be cephalopelvic disproportion, that the cervix be fully dilated, that the membranes be unruptured, that there be no placenta previa, that the uterus be not hypertonic nor already injured. Under these conditions we believe that Potter's technique is not surpassed.

The patient is deeply anesthetized to produce uterine relaxation; the internal hand, the palm of which faces the baby's belly, is introduced gently between the uterus and membranes, stripping the latter up gently without rupturing them. The placenta, if approached, is of course avoided. The head is disengaged and pushed to the side toward which the back lies, at the same time that the external hand pushes the breech to the opposite side. The arms are felt and if necessary effort is made to fold them properly in against the chest. The uterus being relaxed, and the fetus floating in the amniotic fluid, the manipulation described brings the belly and limbs of the child dependent. The membranes are now ruptured and *both* feet seized and brought down through the cervix. Under these conditions, extraction may be carried out forthwith. Gentle, steady traction downward and backward is made on the legs and thighs. The breech will tend to come down posteriorly. But after it is delivered, continuation of traction in the same direction will tend to rotate the torso spontaneously and one or both shoulders will swing under the symphysis. *No pressure* on the fundus should be made during this process. Not until one or both scapulae appear beneath the symphysis is attempt made to deliver the arms. Then stroking of the exposed anterior scapula toward the midline of the baby's body will generally disengage the arm. By slight rotation of the torso and a repetition of the maneuver the other arm is delivered. Then, with the internal hand flexing and guiding the head, the outer hand making gentle traction on the shoulders, and the assistant now gently pressing and guiding the head into the inlet by suprapubic, not fundal, manipulation, the head is extracted.

Necessitous version will, however, frequently have to be done when membranes are ruptured, when the head is rather tightly wedged into the inlet, when an arm is prolapsed, when the uterus is tonic and clamped down on the fetus. Its perform-

ance under such conditions must always be most seriously weighed, and avoided if possible. But if it must be done, the technique is much more difficult and must vary from that described as conditions make necessary. The prolapsed arm must be secured, as a rule, by a sling before proceeding. Again, deep anesthesia is essential to relax the uterus. But the baby will not float freely in the amniotic sac. Patient, gentle, prolonged manipulation may be needed to disengage the head from the lower segment. Both feet may not be accessible, and only one, preferably the anterior, may have to be brought down; even this may require placing a fillet on the ankle before it can be accomplished. Arms, in spite of care, may extend, or wrap themselves around the neck and require patient deft work to disengage them.

Anticipating troublesome possibilities, prior provision should in every case be made of hot moist towels to protect the baby during extraction; of abundant sterile green soap for lubrication incident to all manipulation; forceps to use should the aftercoming head be impacted; oxytocics to control inertia; facilities for cervical repair; means of efficient fetal resuscitation; donors and apparatus for blood transfusion; equipment for craniotomy should the baby succumb during the operation and the head be stubbornly impacted.

The operation is a dangerous one. For the baby, there are the dangers of all breech extractions, besides those sometimes inherent in the maternal indication for the operation. For the mother, there are the dangers of the original indication in some cases plus the grave risk of lacerations of the cervix, the uterus, and contiguous tissues. There is no method of delivery save cesarean section which so thoroughly invades the uterus. The infective danger inherent in such invasion always attends this operation.

We have analyzed 221 cases of combined version from our clinic. Table I exhibits the indications and the results in mortality.

TABLE I  
COMBINED VERSION  
(None Elective)

Indication	Number	Maternal Deaths	Per Cent	Fetal Deaths	Per Cent
Extraction of second twin	45	0	...	1	2.2
Transverse presentation	41	1	2.4	13	30.0
Placenta previa	35	1	2.0	16	41.0
Prolapsed cord	31	0	...	11	35.0
Impacted cephalic presentation	25	0	...	8	32.0
Face presentation	12	0	...	3	25.0
Abruptio placentae	11	0	...	8	73.0
Prolapsed arm	9	0	...	5	44.0
Toxemia after bag induction	8	0	...	1	12.5
Brow presentation	5	0	...	2	40.0
Totals*	221	2	0.9	68	30.8
	177	2	1.1	67	38.0

\* If the practically elective use of the operation for expedition of delivery in twin pregnancy is eliminated, the totals would be as shown on the lower line.

The tremendous fetal mortality was, of course, not directly due to the operation. Prematurity and the effects on the babies of the primary conditions, such as separation of the placenta, prolapse of the cord, placenta previa, were chiefly responsible for the mortality. It probably could not have been very significantly lowered by different handling. However, 25 per cent of the fetal deaths were definitely due to intracranial hemorrhage; one craniotomy was performed; in one case there was traumatic infiltration of kidney and adrenal. All these were attributable to the operation.

TABLE II  
MATERNAL COMPLICATIONS

Severe postpartum hemorrhage	16	
Definite laceration of cervix	15	
Endo- and parametrial infection	6	
Rupture of uterus	3	30
Total serious morbidity	40	13.6 per cent

All maternal complications (Table II) may be attributed to the operation, as those hemorrhages dependent on conditions for which the procedure was employed are eliminated. One of the two maternal deaths, a rupture of the uterus, is directly chargeable to the operation.

Version, as initially defined herein, is an operation of venerable antiquity with a most respectable record of great usefulness;

calling upon the best technical capacity of the obstetrician in performance; capable of brilliant and satisfactory results when properly employed; but embodying great dangers and therefore requiring the most careful and experienced judgment in its application.

#### BREECH EXTRACTION

Breech presentation is that condition in which the breech or buttocks end of the fetal ovoid first approaches the pelvic inlet at the onset of labor. Of its varieties, "frank breech" presentation designates the extended relation of the legs to the fetal body; "footling" the flexion of the legs on the thighs, with or without extension of the thighs, so that the foot or feet precede the buttocks in their passage of the inlet, or come down with them.

If all conditions are favorable, breech presentations, like cephalic, are capable of spontaneous delivery. The obstetrician will, when the termination of spontaneous delivery is imminent, *manage* the delivery, in regard to protecting the perineum, employing episiotomy where indicated, maintaining head flexion, protecting the cord, making traction on the shoulders, and guiding the extrusion of the arms, exactly as in his management of vertex deliveries. This does not constitute interference with a normal process, or "assistance" in any special sense. The term "assisted breech delivery" is in our opinion loosely defined and meaningless.

If there are factors of obstruction to the passage of the fetus, interference, as by manual correction of relation of parts, manual or forceps traction, and so forth, will be necessary as in similar situations in relation to cephalic presentations. These all constitute operative interference, and should be designated by appropriately descriptive terms.

Inasmuch as the great preponderance of cephalic presentations is determined by the resistances of the normally tonic uterus applied to the fetus, any influence which alters these factors, such as flaccidity of the

uterus, over-distention thereof by polyhydramnios or multiple pregnancy, distortion of its cavity by tumors or placenta previa, abnormalities in proportion of the fetus, is prone to cause breech presentation. It may even occur where no ascertainable cause can be assessed. It occurs in earlier stages of pregnancy in many cases which later present by the head. This accounts for the high proportion of breech presentation in prematures.

The mechanism of labor in breech presentation tends to present exactly the same phenomena as in cephalic presentation. However, as the dorsolumbar portion of the fetal axis is not so conveniently jointed as the cervico-occipital portion, the evolution of this mechanism is not so perfect in breech as in cephalic presentation. This fact, together with the relative inadequacy of the soft amorphous breech as a dilator, in comparison with the firmer, better shaped head, makes these presentations more tedious and difficult for the mother.

They are especially hazardous for the fetus for three principal reasons. First, as stated, they frequently attend other abnormalities unfavorable to fetal survival, especially prematurity. Again, delay in the delivery of the head after that of the torso induces asphyxia because the fetus is, in general, unable to respire during this interval. This situation has no parallel in cephalic delivery. Finally, and most important, the liability to intracranial damage is much greater in aftercoming than in forecoming heads. This is because all the pressure necessary to mould the head has to be compressed into a few minutes instead of being spread over several hours. It is the difference essentially between concentrating a certain amount of force or trauma into the equivalent of a sudden blow, and spreading it out in a series of relatively gentle intermittent pressures.

In the management of breech presentation, external cephalic version has prophylactic worth. There is some difference of opinion as to the optimal time for this

effort. We think the completion of the thirty-sixth week is best. It can be successfully accomplished in approximately 60 per cent of cases. It must always be *most gently* done and the fetal heart action must be closely watched. It is best to do it without anesthesia, so that the patient's subjective discomfort may limit the force employed. *Don't hurt the patient. Stop at once* if fetal heart tones indicate distress. Try to rule out placenta previa before undertaking version.

If the case goes into labor in breech presentation, the management should in general embrace the same expectant attitude as in cephalic presentations. All preparations for emergency should be made as discussed under version. The perineum may be protected by episiotomy and by support of the breech as it is extruded.

When the breech is fully born, the legs, if extended along the torso, may be gently flexed and brought down. Deliver the upper torso and shoulders as described under version. Do not hurry this stage. While the safe time for completing delivery is actually limited, it is better to be gentle than to gain time by damaging, forceful haste.

The head in these situations never has had the advantage of partial moulding as it frequently has where extraction follows version, whereas the baby is usually full grown and in good condition. The manipulation of the head, therefore, calls for even more finesse than where version has been done. It should be well flexed, and brought through the inlet approximately in the transverse axis. Rotation of the occiput forward should be done only when the head is well down in the pelvic cavity.

If the passage of the inlet is not easy, prompt resort should be had to the application of forceps, rather than reserving this resource for attempted extrication of a head already badly traumatized by over-zealous manual traction. The special forceps of Piper is a facile instrument, but any good type of forceps may be used. Once the face is exposed in the vulva so that access

of air to the infant's lungs is established, there is no further necessity for haste and the resistance to the passage of the head over the pelvic floor may be deliberately managed.

In premature babies delivering by the breech, special caution should be employed. The relatively slender body sometimes slips through a poorly dilated cervix. Give the cervix time to dilate spontaneously. The slender chance of saving a questionably viable infant is not worth the risk of cervical damage consequent on hurried extraction.

In 20,000 deliveries in our clinic there were 859 breech presentations, an incidence of 4.3 per cent. Of these, 675 were full term. With reference only to the term cases, fifty-one babies were stillborn, while an additional twenty-five died in the neonatal period. In percentages, this is a fetal mortality of:

	Per Cent
Stillbirths.	7 5
Neonatal deaths	3 8
	<hr/>
Total	11 3

This compares with the average percentages of fetal mortality of:

	Per Cent
Stillbirths	2 41
Neonatal deaths	2 46
	<hr/>
Total	4 87

The divergence well exhibits the increased fetal risk of breech delivery. This risk depends most on the direct mechanical injuries involved, i.e., intracranial hemorrhage, with or without fracture of the skull, and trauma to other viscera.

Forceps and cesarean section were the principal methods of operative interference, representing 19.5 per cent and 2.3 per cent incidence respectively. These figures are not significantly different from the incidence of these procedures in cephalic presentation. A craniotomy incidence of 1 per cent was, however, distinctly higher than the incidence in cephalic presentation.



There was no maternal mortality attributed to breech presentation per se.

#### SUMMARY

1. Podalic version is discussed without reference to its so-called "elective employment."

2. Its indications are detailed, showing that its use even for necessitous conditions is not so frequent as in the past, due to the availability of other delivery procedures.

3. The technique of its performance is briefly outlined, with emphasis on provision of resources for handling complications.

4. It is pointed out that the operation represents distinct hazards both to the mother and baby. Data of 221 cases are furnished, showing an average fetal mortality of over 30 per cent, principally still-

births, which is more than ten times the stillbirth rate for the whole material of the clinic. One-quarter of this stillborn rate is due to intracranial damage. Maternal death is occasionally directly dependent on the operation. High incidence of grave maternal complications follows it.

5. Breech presentation, its frequency of occurrence, its principal causes, and certain principles of mechanism are discussed, and the hazards for the mother and fetus are outlined.

6. The management and technique of delivery are described.

7. The ratio of stillbirth and neonatal death incidence in this presentation are compared with the average ratio in the whole mortality of the clinic, and shown to be more than twice as high as the latter.



# THE USE OF THE OBSTETRIC FORCEPS

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THE obstetric forceps, like the automobile, may be indispensable, if properly used, in the saving of life and human effort and suffering; and, improperly used, it may be the instrument of many unnecessary deaths. There are six principles essential to the safe and successful use of the forceps:

1. The cervix must be fully dilated, that is, its passage must be large enough to slip over the head at the plane of maximal diameters without retarding pressure. It is very easy to let one's obstetric conscience slip in this direction until, by degrees, it becomes habitual to apply the forceps when the cervical passage lacks 2 or even 4 cm. of complete dilatation. It should be remembered that a rim of cervix 1 cm. wide diminishes every diameter of the passage by 2 cm. Dragging the head through this inadequate opening results at least in laceration of the cervix, and at most, in fatal intracranial strains and resultant hemorrhage.

2. The forceps must be properly applied. It may be difficult (in rare cases, impossible) to apply the forceps symmetrically to the head, but repeated attempts should be made until the sagittal suture coincides with the vertical plane of the forceps. Failure to effect this adjustment accounts for most of the cases of slipping of the forceps. Properly applied, it is almost impossible (impossible within the justifiable limits of force of traction) to pull the forceps off the head. Improper application results in a mechanical maladjustment somewhat like using the wrong wrench on a bolt-head—the wrench is almost certain to slip, or to hold only because of damage to the bolt. Pressure injuries to the soft parts of the fetal head may be inevitable; but

gashes and tearing off of ears, lips, etc., should never occur.

3. Force in the application and adjustment of the forceps is never permissible. If difficulty is encountered, something is wrong—the position of the head has changed, the forceps has slipped outside of the cervix instead of inside it, the blade has caught against an ear or some other prominence, or the whole route of the introduction of the blade has been wrong. Proper introduction of the forceps involves a knowledge of the topography and axis of the birth canal, and requires a technique of letting the blade follow the line of least resistance (as in sounding of the urethra). Any attempt at forcible steering is apt to lead the top of the blade into a hopelessly blocked situation. It is better to dislodge the head and change its position than to attempt to force the forceps past any serious obstacle.

4. The head should never be compressed by squeezing on the handles of the forceps. It is very easy, in making traction, to apply great lateral pressure on the head by involuntary squeezing. Once a snug and accurate fit of the blades has been accomplished, nothing is gained by further compression: in other words, excessive compression adds no security against slipping.

5. Force in extraction should never be employed. It is difficult to estimate the tractive force which one employs in actual practice, so that dynamometric figures are of no great practical value. Force sufficient to move the patient on the table is excessive. Moderate traction will cause the pelvis to slide on the fat of the buttocks, so that, especially in obese individuals, the apparent to-and-fro movement of the pelvis may be quite great; but the buttocks

should never slide on the pad, nor the pad on the table. The whole secret of forceps-traction lies in a reproduction of the effect of a strong expulsive effort. To attempt to accomplish the second stage of labor in one terrific pull creates destructive stresses and strains on the intracranial architecture. Rather, one should aim, by repeated pulls, with a rest of at least a minute between each pull, to reproduce natural labor. This permits moulding to occur, and facilitates the natural adaptation of the head to the contours of the pelvis with resulting necessary changes in the position of the head. It is far better to expend an hour or more in securing an undamaged baby than to terminate the process rapidly at the cost of the baby's life. An effective safeguard against excessive traction is offered by having the operator sit on a stool without bracing his feet against the floor (to say nothing of bracing them against the delivery table).

6. The mechanics of forceps delivery must reproduce the mechanism of labor. This, of course, requires a knowledge on the part of the obstetrician for the diagnosis of fetal position; of the landmarks of the presenting part; of the pelvic contours at the various levels; of the necessary elements of rotation, flexion, and extension; and of the axis of the birth canal. In a brief paper, it is impossible to enter into the detail of all these elements. It must suffice to say that the exact position of the presenting part must be determined; that a proper cephalic application of the forceps must be made; that the head must be flexed and rotated until the plane of its maximal diameter lies in the most favorable relation to the diameters of the pelvic plane involved; that traction must be made in the axis of the birth canal; and that the elements of rotation, flexion, and direction of traction must constantly be changed as the head descends. Such a technique is very different from that all too commonly seen, in which the instrument is forced into some sort of a pelvic application, without any attempt to check up carefully after the

application, and by which the delivery effected by continuous horizontal traction of a violence limited only by the physical strength of the operator.

*Episiotomy.* The role of episiotomy in connection with forceps is a dual one. In the application of forceps above the mid-pelvic level in malpositions, a preliminary episiotomy will often greatly facilitate the introduction and placement of the blades. Still more important is the commonly overlooked factor of the elimination of the added pressure upon the fetal head created by the dilatation of the introitus. Episiotomy is commonly regarded as a safeguard to the mother and yet the worst that can happen to her in the absence of episiotomy is an extensive reparable laceration, while the added pressure in perineal dystocia or in forceps extraction may cost the baby its life. In the major forceps operations, the traction and relatively rapid moulding has created an excessive intracranial strain by the time the head reaches the perineum; and the added pressure involved by using the head as an introital dilator may easily become the straw that breaks the camel's back.

*Levels of Application of Forceps.* There seem to be no generally accepted definitions of the terms "high," "mid," and "low" forceps. For the purposes of this discussion, the following definitions are used: "High forceps" means the application of forceps when the plane of maximal cephalic diameters (in the existing cephalic attitude—not necessarily the strict anatomic plane of maximal diameters) lies in the plane of the pelvic inlet. "Mid forceps" means the same in relation to the plane of maximal diameters and "low forceps" the same in relation to (or below) the plane of minimal diameters. There are of course, intermediate stations at which the forceps must be applied. For practical purposes, a rough estimate of the level of the plane of maximal diameters can be made from the level of the vertex, which lies more or less one station below the plane occupied by the plane of maximal diameters: in high

forceps the vertex is above the ischial spines; in mid forceps it is at the level of the spines; and in low forceps it lies against the pelvic floor or at the plane of the outlet. "Floating forceps" is an obsolete procedure, version and extraction being by far preferable.

1. The *low forceps* is the simplest application and hence may serve as a starting point. With rare exceptions the position is occipito-anterior within a range of about 30 degrees to either side of the sagittal plane. If the perineum has been somewhat distended, the sagittal suture usually lies in the sagittal plane of the pelvis. It must be remembered that with each recession of the head marked rotation may occur, especially as anesthesia is deepened for the actual application: hence it is necessary to re-orient the head at the moment of application of each of the blades, and to re-check the entire situation before and after locking the blades. With everything in order, traction is made as described in the first section of this discussion. The direction of traction varies with the level at which the plane of maximal cephalic diameters lies—at a point just below "mid forceps" the traction is outward and slightly backward; as the head impinges upon the perineum it is directly outward; and as the head distends the perineum and emerges from between the tubera the traction has more and more of a forward trend until, as the occiput slips from under the pubis, the traction is almost directly forward. If episiotomy is done, the perineal stage of labor is eliminated and the head is delivered by direct outward traction until the occiput slips out from under the pubis. If the perineum is allowed to remain intact, a great many operators remove the forceps from the head as the occiput disengages, and express the head through the introitus by pressure through the distended perineum from behind. My personal conviction is that the head is better controlled by not removing the forceps, and that the presence of the instrument (if

properly managed) adds nothing to the risk of perineal laceration.

2. The *mid forceps* is almost always a "forceps operation of necessity," in contradistinction to the low forceps, which is usually "elective." Episiotomy will ordinarily eliminate the necessity for low forceps; but, since the mother must recover from the deeper anesthesia required for an episiotomy before the resumption of effective contractions and expulsive efforts, the considerable lapse of time involved (except under gas anesthesia) justifies the elective low forceps operation. The application of forceps in the mid-pelvic levels, on the other hand, involves a certain risk to the fetus which increases rapidly with the height of the head. Mid forceps, therefore, is not justifiable unless the risk to the fetus is less from the forceps than from permitting the head to remain in situ. The six principles enumerated in the first part of this discussion must always be kept firmly in mind and rigidly observed.

(a) Simple arrest of the head in an occipito-anterior position. This is usually due to one of two things: incomplete dilation of the cervix, or insufficient moulding in cases of cephalopelvic disproportion of either type (large head or small pelvis). In a few cases the arrest may be due to contraction or deformity of the middle and lower pelvis. It is obvious, in either case, that the decision in favor of application of the forceps should not be made hastily. Extreme care should be taken to be certain that the cervix is really completely dilated; if it is not, more time is required. If the head is arrested solely through disproportion or moderate extension, time again affords the only safe means of adaptation of the head to the pelvis. Time is the most valuable instrument in the obstetrician's armamentarium. I once heard the late Dr. Ross McPherson say: "Gentlemen, have you ever noticed the ease with which the consulting obstetrician delivers the difficult case?"—meaning that the time which has been required to bring the consultant to the bedside has permitted the natural

forces to convert the difficult into an easy case. In such situations it is generally best to wait half an hour after the decision to apply the forceps has been made.

(b) Persistent occipitoposterior positions and transverse arrest. In these situations we have not only a disproportion of adaptation, but an increase in dystocia on account of the tendency of the head to extend. It is difficult to define exactly the term "persistent." Probably in about half of all cases the head enters the pelvis in the transverse or posterior position, and natural adaptation brings the head into the anterior position in the mid-pelvic levels in all except a small percentage of cases. It is better to permit this process to occur, because there is less trauma to the head and to the maternal soft parts, and because no element of potential infection is introduced. As long as there is no undue extension, and the head fits loosely in the pelvis, forceps should not be employed. On the other hand, increasing extension or impaction create a situation which cannot be solved by nature without a marked risk of intracranial damage, and early use of the forceps is indicated. In rather rare cases, trachelotomy (Dührssen's incisions) may be necessary to the favorable outcome of the case.

The introduction and placement of the blades may be difficult, but this does not justify a haphazard application. Much more than in low forceps is the proper application necessary. One may be guided to some extent by fixed rules, but in numerous instances the orthodox rules must be abandoned and a technique adapted to the case invented. My own rule in such cases is to apply "the more difficult blade" first, since the absence of the other blade gives more room for maneuvering the first. Having the buttocks an inch or two beyond the end of the table facilitates greatly the application of the anterior blade; in rare instances a preliminary episiotomy makes a great deal of difference. The first blade should be placed as accurately as possible, although it is almost

certain to be dislodged to some extent during the introduction of the second blade. When both blades are in place, their accurate placement in relation to the head should be effected; whereupon the problem (often difficult) of accurate locking frequently arises. The blades should be manipulated in and out with the greatest gentleness and with the mental eye fixed upon the tips of the blades with regard to the various curves of the forceps, the head, and the available cephalopelvic spaces. After locking has been effected, the cephalic application must again be checked and corrected if necessary.

In rare instances it may be necessary to employ the Kielland type of forceps. If any of the standard types of forceps is employed in cases of transverse arrest, a normal application should be made so that reapplication after rotation will not be necessary. In posterior positions, of course, a reverse application must be made, with reapplication after rotation.

The rotation is best effected by Bill's modification of the Scanzoni maneuver: the handles must be deflected in the direction of the sinciput (for the sake of whatever flexion is possible) until the long axis of the blades coincides with the axis of the pelvis; the tips of the handles are then swung in a circle of a radius sufficient to keep the axes of the blades and of the pelvis coincidental. It is a good plan, if possible, to overcorrect slightly (the sagittal suture being rotated a little past the sagittal plane of the pelvis) and to have an assistant grasp the body of the fetus from above in order to lessen the tendency to backward rotation as the blades are removed. I find it much simpler to employ two pairs of forceps, and to apply the first blade of the second forceps before removing the second blade of the first forceps (Tucker-McLain for rotation, Elliott for extraction). Of course, if the Kielland forceps is used, reapplication is generally unnecessary. Traction must be made along the axis of the birth canal, backward and downward, merging with progress into downward until the outlet is

reached, when the traction of low forceps is employed.

3. The use of *forceps on the aftercoming head* in breech presentations is one of the most life-saving procedures in obstetrics. Relieving, as it does, the strain on the cervical spine and the great nerve plexuses, it also affords a means of steering and flexing the head and an opportunity of providing an airway to the nose and mouth of the fetus which may be utilized when the extraction of the head must be made slowly in order to avoid the intracranial damage incident to excessive pressure and rapid moulding. Episiotomy is almost essential, although where the perineum is apparently elastic enough, episiotomy may be deferred until the need for it becomes apparent. For the obstetrician working without an assistant, especially in the home, it is probably best to perform a preliminary episiotomy. Before applying the forceps the patient should be brought down until the buttocks project at least 2 inches over the edge of the table or bed because, since the procedure is essentially a high forceps, the initial traction must be made directly backward. As soon as the arms are delivered, and before any traction comes upon the head, two fingers should be introduced under the fetus to the lower part of the face: whereupon gentle manipulation will flex the head into the most favorable attitude and steer the chin into the more convenient posterior oblique diameter of the inlet. If the head is jammed in the inlet it may be dislodged by pushing the body of the fetus upward. Flexion and position must be maintained by the fingers while the blades are applied with the other hand.

The orthodox application is made from beneath the body of the fetus, which is held forward and out of the way by an assistant. (Care should be taken to avoid hyperextension of the neck, which may cause serious injury.) When working alone, the obstetrician will find it much easier to apply the forceps over the shoulders of the fetus from behind its back, the body being

allowed practically to dangle vertically. In some cases this application will be found to be much easier than the orthodox one, since the tips of the blades can be introduced immediately along the base of the skull on each side, and allowed to follow the contour of the head under direct visual inspection. After checking the application, traction should be made in the axis of the superior strait, i.e., almost directly backward (toward the floor). If disproportion offers an obstacle, an airway to the fetus may be provided between two fingers or, better, by introducing a Sims speculum along the posterior wall of the vagina and wiping or sucking the fluids away from the nose and mouth. Provision of an airway permits one to take as much time as is necessary for safe moulding of the head. As the head descends, the direction of traction is of course altered to follow the axis of the birth canal.

There is a final point which requires a brief discussion, that is, whether signs of distress in the fetus, as evidenced by rapid, slow, or irregular heart action, should be considered as an indication for immediate delivery. It must be remembered that fetal distress of this type is evidence of either shock or intracranial pressure and that rapid delivery is apt to increase greatly and abruptly the underlying causes of the pathologic status. In other words, rapid delivery may determine a fatal issue which might have been avoided by leaving the forces of nature to their gentler and slower solution of the problem. This is especially true in cases where the fetal distress is brought about by excessively powerful uterine contractions or bearing-down efforts on the part of the mother. In such cases slowing of the labor by anesthesia is the only reasonable treatment. If the distress becomes manifest in the low position, episiotomy and forceps (if necessary) constitute the best solution. If the head is at a level higher than mid-pelvis, if the cervix is incompletely dilated, or if disproportion exists, it is better not to employ the forceps. Malposition of the

head should be corrected, using the forceps if necessary; but it is frequently best, in such cases, not to employ the forceps for traction, until the condition of the fetus has markedly improved. It is in the mid-pelvis that the greatest care and judgment in regard to the employment of the forceps become essential. If in doubt, leave the situation alone.

#### CONCLUSION

The obstetric forceps properly used is one of the most valuable of all instruments; improperly used it may be productive of disaster. The foregoing discussion is an attempt to summarize the principles and rules which help to eliminate the risk involved in the improper use of this instrument.



WOMEN, for one cause or another, and there are many, may become so accustomed to a leukorrhea—a discharge from the uterus or vagina—that they altogether ignore the suggestively odorous, pinkish discharge of early cervical cancer.

From—"A Textbook of Surgery" by John Homans (Thomas).

# INJURIES AND REPAIRS OF THE BIRTH CANAL DURING LABOR

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PHILADELPHIA, PENNSYLVANIA

IN the practice of obstetrics, the commonest abnormality with which we have to deal is laceration of the structures of the parturient canal. The usual and most accepted classification of these lacerations is in the two divisions of perineal and cervical.

The perineal lacerations are divided into three types: first degree—lacerations of the mucous membrane of the vaginal canal only; second degree—including lacerations of the muscle structures of the perineal body and rectal sphincter; third degree—or complete lacerations which involve the rectovaginal septum to the degree of entering the lumen of the rectum.

It is an understood fact in obstetric teaching today, that if nature were permitted spontaneously to deliver a primiparous mother of a single child, in the vast majority of cases, one of the three types of laceration would result. However, these lacerations may occur even after every precaution has been taken, and it is only necessary to examine the birth canal of a multiparous patient to realize that serious damage may be done to the supporting structures with resultant relaxation and formation of rectocele and cystocele.

Lacerations of the posterior vaginal canal are more common than anterior ones. The integument may not necessarily be affected, as frequently the supporting structures, particularly the fascia, relax sufficiently during the passage of the child through the birth canal, so that the mucous membrane of the vagina escapes injury. Anatomically, the anterior portion of the vagina is much shorter than the posterior portion and is less likely to become injured, if the cervix is allowed to

become fully dilated and effaced before any operative procedure is attempted.

The mechanism of labor in breech as well as vertex presentation consists of rotation, flexion, molding and descent, all of which are essential in guiding the passenger's approach towards the vaginal outlet.

All lacerated areas, even those of minor or first degree type, are potentially infected by the normal vaginal flora which may become pathogenic in traumatized and devitalized tissue. The possibility of infection increases materially with the extent of the injury. Lacerations may be single or multiple, and may occur in the anterior, lateral, or posterior walls. However, operative delivery and intervention, if not attended with every precaution, are very prone to increase the number and severity of these lacerations. There are some obstetricians who are firm believers in operative delivery, as they feel better able to prevent injuries to the birth canal when the passenger can be instrumentally guided and controlled.

Injury of the birth canal is particularly associated with primigravidae, and one of the best preventive measures is the allotment of adequate time to permit these structures gradually to relax and not be forcibly overstretched, lacerated, or torn by too hasty a delivery procedure. As we consider the perineal body, the transversus perinei, and levator sphincter ani to be the supporting structures, it should be our aim to prevent injury of these parts whenever possible.

In recent years we have learned that it is a safer and wiser procedure to incise or cut into the perineal body, rather than permit it to be lacerated voluntarily. This incision is



termed "episiotomy." When this procedure is followed, the tissue can then be repaired primarily and widespread trauma avoided. It is a well recognized fact that traumatized tissue is a fertile field for local infection and that a more satisfactory result is obtained if tissues, muscle, fascia, and vaginal mucous membrane are untraumatized. Episiotomy has met with such good results that it is now almost routine in every well regulated maternity hospital where sufficient well trained and competent physicians are present to perform outlet forceps operation, prophylactic forceps, or breech extraction, and to properly repair episiotomy upon completion of delivery.

All lacerations of the birth canal should be subjected to primary repair, which means immediately following delivery of the child, if the patient's condition warrants a short continuation of an anesthetic, which is necessary to accomplish this procedure. This applies to the more extensive injury of rectovaginal septum and complete lacerations involving the sphincter muscle and lumen of the bowel, as well as minor lacerations.

Prevention is the keynote of success and it is in the interest of the birth canal structures that episiotomy with forceps extraction of the vertex, or episiotomy with breech extraction, is advised in all primiparous patients and many multiparous individuals.

Injuries to the clitoris and urethra are occasionally met and the bleeding associated with these is often excessive in amount. All bleeding points in the vaginal area should be noted and controlled. This may be done by suture or ligation. It should be distinctly understood that it is imperative for the operator performing the repair to return the structures to their original anatomic position. There seem to be several very erroneous ideas prevalent, relative to repair of vaginal injury. In episiotomies as well as in spontaneous lacerations of any degree, repair must be undertaken with several important facts in mind, namely, unsatisfactory results are usually due to

(1) improper technique in preparation of patient; (2) poor apposition of the structures; (3) too heavy or too much suture material, whether absorbable or non-absorbable; (4) too securely knotted sutures which restrict drainage as well as circulation.

Primary union should be our aim and primary repair should be instituted whenever possible. It is truly remarkable, however, that fairly satisfactory, and occasionally very satisfactory, results may be obtained even though poor apposition and incompetent surgical technique have been used. This method and the method of allowing the structures to approximate themselves without repair, are not advocated.

After-care of perineal lacerations is equally important in accomplishing good results. All suture material and the areas about the vaginal canal should be scrupulously cleansed, dried and protected at frequent intervals. If evidence of infection is manifested by edema, redness and tenderness, application of a hot, wet, surgical dressing is preferable to removal of the sutures.

Absorbable perineal sutures are advocated in the repair of these lacerations in most instances. It has been proved that silver wire, silk, linen, and silkworm gut, have a tendency to cut through tissue because of their inability to yield to the structural and histologic changes in the healing process. Absorbable sutures are more satisfactory because of their elasticity and flexibility.

It is very important that lacerations of the birth canal must not be approximated too tightly, as in all these tissues during the process of healing there is serum present and lochial materials flowing over both the mucous membrane and integument surfaces. A wound that is sealed too tightly, as is the practice followed by some in using a subcuticular perineal stitch, is very likely to collect pockets of secretion which may eventually become infected and result in local inflammatory reaction. One of the most eminent obstetricians in the country

has stated, and it is a good thought to remember, that if all sutures were tied over a hemostat, better and more satisfactory results would be obtained.

The end-results of repair of the birth canal should include complete restoration of the sphincter and bowel control, in the third degree lacerations; a supporting and flexible perineal muscle sling in the second degree lacerations; and an even and smooth union of the vaginal mucosa in those of minor or first degree.

Primary repair is advocated, if possible. However, if a patient's condition does not warrant repair immediately following delivery, intermediate repair should be carried out, at which time the same general principles should be followed as in doing primary repair. Five to seven days postpartum seems a sufficient length of time between delivery and intermediate repair. If at the end of this time intermediate repair is contraindicated, secondary repair may be done following the termination of the puerperal state. It is wise not to postpone secondary repair too long, particularly in third degree lacerations, as retraction of the sphincter within its sheath often causes some difficulty in its proper apposition and adjustment. The rectal wall is likewise more difficult to approximate and the formation of scar tissue tends to poor healing and union and increases the possibility of a breakdown of the repaired structures.

In rectovaginal fistulae and complete tears of the perineum, it is often wise to proceed with severance of the sphincter muscle by incision in its posterior portion, in order better to approximate the retracting ends. This seems to relieve a great deal of discomfort and pain. Particular attention must be paid to the residual material collecting in the rectum above the sphincter repair.

In postoperative care and treatment, the diet is of importance. Liquid and non-bulky diets should be adhered to. Liquids should be given for the first three or four days and proper enema and postoperative bowel

technique, such as rectal instillations of oil, as well as oral administration, should be carried out to obtain the best results. Sphincter control is brought about occasionally by formation of scar tissue, but in most instances this cannot be considered a satisfactory result.

Repairs of the urethra should be accomplished as a primary operation and satisfactory results may be obtained if an indwelling catheter is placed in the bladder for from three to five days.

Vesicovaginal fistulae and vesical lacerations should be immediately repaired. Indwelling catheters and proper irrigation of the bladder should be instituted for one week postpartum. Particular attention is directed towards the free escape of bladder fluid through the catheter, which is necessary in order to avoid distention of the bladder before primary union has taken place. This usually occurs one week to ten days postoperatively.

All external lacerations such as lacerations of the labia minora, labia majora, and episiotomies, whether they be median, mediolateral, or lateral, can be accomplished as described in repair of the primary lacerations of the birth canal.

The cervical lacerations vary in number and extent and may be unilateral, bilateral, single or multiple. There is seldom, if ever, a birth through a nulliparous cervix which does not destroy some of the continuity of the cervical structures, either the external or internal os, or cervical canal. Small cracks or nicks in the cervical mucosa which do not cause profuse bleeding can be demonstrated in almost every puerperal cervix. Primary lacerations can be prevented to a great extent by allowing sufficient time for the cervical canal to become effaced and the cervical os completely dilated. Forceful dilation is in error except where indications point to a dystocia of the cervix or where it is necessary to dilate the cervix rapidly in the interest of either mother or child. Accouchement forcé, forceful dilatation of the cervix and extraction of the child, is responsible

for very damaging injury to the pelvic structures.

The accepted classification of cervical injuries is: first degree or primary lacerations—small endometrial or mucous membrane tears; second degree—lacerations in the cervical canal up to the internal os, unilateral, bilateral, or stellate in type; third degree—lacerations which enter through the internal os and extend up to the fornices of the pelvis and very often into the lower portion of the broad ligament.

It is not always advisable to suture the primary lacerations if they are not bleeding at the time of inspection of the cervix. Prevention of these injuries is necessary at all times. No operative procedure through an undilated and uneffaced cervix is ever justified. Forceps delivery through an undilated cervix is not only dangerous but is considered very poor technique. Dilatation of the cervix and internal podalic version may be accomplished without severe injury to the cervix if sufficient time is allowed for gradual and complete manual dilatation. Great damage is done when manual dilatation is not completed before internal podalic version is attempted. Artificial delivery with partial dilatation is usually the cause of the extensive lacerations of the cervix which fall under the third degree type. Extensive hemorrhage occurs and extension of the laceration may enter the pelvic portion of the abdominal cavity as well as the corpus of the uterus.

Following all procedures, such as manual rotation of the vertex, internal podalic version or Braxton Hicks' version, or forceps delivery in transverse arrest of the head and posterior positions, the cervix should be inspected. In every instance where the uterine cavity has been invaded to facilitate delivery, as in abnormal positions, transverse arrest, and breech extractions, inspection of the cervix and immediate repair of lacerations present is advisable.

The same principles apply in the repair of lacerations of the cervix as in lacerations of the perineum. Hemostasis as well as

approximation of the tissue is the primary aim. As the hemorrhage is often excessive, deep and full sutures are occasionally required, tightening the sutures only sufficiently to approximate the structures and control the hemorrhage.

Inspection of the cervix is at times a rather difficult procedure and therefore every delivery room table set-up should be equipped with the proper specula for viewing cervical areas and proper sponge forceps to be used as a tenaculum. The cervical tissues are soft, friable, often edematous, even at times hemorrhagic, and severe injury can be done by tearing cervical structures with the tenaculum. Retraction of the vaginal canal with the proper speculum makes the drawing down, inspection, and suturing of the cervix a simpler procedure. It is very distressing to inspect the cervix after delivery and try to realize that this seemingly badly traumatized cervical area could ever regain its normal appearance. It is truly marvelous to discover upon inspection several weeks postpartum that what seemed at the time of delivery to be a hopeless condition healed through the process of involution and actually is again a satisfactory structure.

Routine inspection of the cervix is not advised unless the bleeding is characteristic of cervical injury or unless some of the operative procedures heretofore mentioned have occurred. Cervical injury can usually be readily diagnosed and can be differentiated from perineal laceration bleeding which is usually dark in color and of more venous character and generally easily visible. Cervical bleeding is definitely arterial in character and there is a constant trickle from the birth canal while the uterus is well contracted. This is in contradistinction to the bleeding from the uterine cavity which is associated with a soft, non-contracting uterus, when the bleeding occurs in gushes through the vaginal orifice.

Intermediate repair of the cervix may be accomplished when necessary during the puerperal state. Secondary operations on

the cervix, or trachelorrhaphy, are not under discussion here.

Frequently extensive lacerations of the cervix extend into the corpus of the uterus. This is accompanied by bleeding into the abdominal cavity and may, if not too extensive, be repaired from the vaginal area. If, however, these lacerations are above the internal os, directly behind the bladder, posteriorly, or in the broad ligament, it is necessary occasionally that they be approached from the abdominal route.

Diagnosis of uterine rupture can be made by palpation from below. Upon examination the hand passes through the uterine wall directly into the abdominal cavity. Supravaginal hysterectomy is usually necessary and all facilities must be at hand and be utilized to replenish blood loss and to combat surgical shock. Vaginal packing and uterine packing may in certain instances temporarily stop the flow of blood from the laceration until the patient can be properly prepared for abdominal laparotomy.

Spontaneous rupture of the uterus has been occasionally reported. Usually there is an etiologic factor of previous endometritis or infection, intramural fibroids, previous operation such as myomectomy, cesarean section, or suspension operation. Particularly must we consider those operative procedures where the convalescence has been febrile and the postoperative course stormy. Reports of spontaneous uterine rupture seem to occur more frequently in those individuals who have had previous cesarean section performed because of cephalopelvic disproportion.

Ruptures of the uterus are classified as complete and incomplete. Some ruptures occur easily in labor while others are the result of protracted and prolonged labors, as well as operative intervention at the time of delivery.

Since Baudelocque, Bandl and many other early investigators gave us a more elucidated picture of this condition and called our attention to the anatomic structures of the uterus, especially the lower

segment, the handling of uterine rupture has been a controversial subject. Today the pendulum is swinging towards cesarean section in the lower segment of the uterus, as the procedure of choice. This brings to mind the controversy of thirty or forty years ago when the lower uterine segment of the parturient canal was brought under closer scrutiny. The older authorities maintained that rupture was more apt to occur during labor, in the lower segment which was the stretchable and dilatable portion, than in the upper portion of the uterus where the musculature contracted. Their supposition was that this contractile portion might prevent the uterus from rupturing. The fundal cesarean section, whether in emergency or electively performed, afforded in their opinion a safer area for healing than would the lower cervical portion of the uterus. Whether the incision was longitudinal or vertical, made little or no difference, but unquestionably the low cesarean section in potentially and infected cases, has reduced the maternal mortality to such an extent that the low operation is now justifiable in these cases.

The extraperitoneal operation as well as the classical type of cesarean section is subject to the accident of rupture in subsequent labors, particularly is this so when abnormal presentations and positions and relatively all absolutely contracted pelves, exert an excessive amount of contractile action on the uterus. Occasionally partial ruptures have been reported where the muscle had separated while the peritoneal covering of the uterus remained intact. Lacerations may be in any portion of the uterine corpus, but complete rupture includes the entire uterine structure. Most ruptures seem to occur in the lateral and transverse areas in the supravaginal region.

The prevention of rupture of the uterus is the keynote of success in individuals whose etiologic factor may be the causative factor. All individuals who have a relatively contracted pelvis must be considered at least potential subjects for repeated or second operations of cesarean section.

When threatened partial or complete rupture of the uterus occurs the patient gives a very definite symptomatology and clinical picture. Uterine contractions cease, constant abdominal pain replaces intermittent uterine contractions, blood pressure falls, pulse rises rapidly, and there is a tender local area. All of these symptoms are forerunners of oncoming rupture followed by surgical shock. Profuse vaginal bleeding may occur through the cervix or massive hemorrhage may occur in the abdominal cavity.

Prompt surgical intervention is imperative. Previous to the onset of an operative procedure to relieve this condition, the general condition of the patient must be immediately considered. Blood transfusions and intravenous fluids are necessary. Operation should not be performed while the patient is in profound surgical shock. It has been reported that the placental structure and fetus have been found in the abdominal cavity extruding through the rent in the uterus and the uterus in contraction when the abdominal cavity was opened. Hysterectomy with immediate control of hemorrhage is advisable in most instances. In a partially ruptured uterus the contents of the uterus may be evacuated and the repair of the rupture performed. Some authorities advocate *porro* cesarean section in partially ruptured uterus or in suspected ruptured uteri. The elective method and decision as to the most advantageous time for operation has been demonstrated repeatedly by the low maternal and fetal mortality. The high maternal and fetal mortality is attributed to those individuals who have had loss of blood, a prolonged labor, and an emergency cesarean section.

If partial rupture of the uterus occurs during dilatation of the lower uterine segment, it is usually confined to that portion of the lower segment and after delivery is accomplished from below through the birth canal, proper tamponade and packing of the uterus may be sufficient to

control hemorrhage. At times temporary methods may be used which allow a more favorable condition to become present in the individual so that blood loss and surgical shock may be combated or prevented before operative procedure is instituted.

The contraction of the uterus between the upper portion and the cervical segment at the area of Bandl's ring, has been responsible for many ruptures of the uterus. When, however, a complete rupture has occurred and the laceration extends into the peritoneal cavity drastic and prompt operation has met with rather unusual success.

As the placenta is usually situated over the old previous scar tissue and there is infiltration of the chorionic villi into the decidua layer of this region, this may be an important factor in the rupture of the uterus after a previous cesarean section.

Prolonged second stage of labor with sudden cessation of uterine contractions and constant lower abdominal pain and tetanic condition of the uterus seems to be indicative of rupture. Bandl's contraction ring can usually be palpated without difficulty and is usually present at or below the umbilical area.

The uterus may be traumatically ruptured during operative procedures, as in *internal podalic version*, in cases of undiagnosed monstrosities, and hydrocephalic infants, where pressure from the intra-uterine fetal structures has caused a necrosis of the uterine wall. Occasionally the fetal structure which has been expelled from the uterus into the abdominal cavity can be clearly felt by abdominal palpation.

Prognosis in complete and incomplete rupture of the uterus is far more favorable now than it was previously, as prevention and prophylaxis against rupture are more clearly understood. We consider uterine rupture which occurs in an individual with the possibility of a suspected rupture, a preventable accident. A careful history will often outline the possibility of rupture.

Previous pregnancies, miscarriages, operations, repeated abortions and curettage, all must be considered in the prophylactic care.

If rupture should occur when the passerger is low in the birth canal, extraction by forceps may occasionally be indicated but should not be undertaken until immediate operative preparation is accomplished.

In the partial and complete ruptures of the uterus many methods of treatment are advocated. Some authorities feel that all incomplete ruptures should be packed while others advocate porro hysterectomy. Some feel that hysterectomy and pan-hysterectomy should be carried out in all cases of complete rupture. No specific

operation can be devised as each case must be individualized.

Maternal mortality in most ruptures of the uterus is attributable to hemorrhage, shock, or sepsis. In the accident of uterine rupture, be it complete or incomplete, premonitory symptoms and etiologic factors are always present and play a most important part in determining the ultimate result. Definitely the prognosis is better if the interval between rupture and operation is of short duration. The less loss of blood, the more favorable the prognosis; the shorter the labor, the better the prognosis; and all immediate treatment at our command must be instituted to prevent accompanying shock.



THE ovary is particularly subject to cyst and tumor formation, a process which is sometimes purely one of retention of fluid and sometimes a combination of retention with actual new growth.

From—"A Textbook of Surgery" by John Homans (Thomas).

# POSTPARTUM HEMORRHAGE\*

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POSTPARTUM hemorrhage is still a major factor in maternal mortality in this country. Although there has been a progressive and an appreciable decrease in maternal deaths during the past five years, deaths from hemorrhage have been little affected, averaging 6 to 6.5 per 10,000 live births. Proportionately, hemorrhage looms as an ever increasing cause of death among the three major causes. These statistics do not tell the entire story, for hemorrhage is often an important contributory factor in the development of puerperal infection. Stander has noted that the incidence of infection in all hospital deliveries is 11.2 per cent, whereas this incidence increases to 27.2 per cent following postpartum hemorrhage. It must, therefore, be noted that some of the puerperal deaths attributed to sepsis must be charged indirectly to hemorrhage. Still another interesting phase of this problem is the fact that serious postpartum hemorrhages are largely preventable and mortality can be eliminated almost entirely. This has been possible in the larger centers and should be possible in general practice.

Bleeding during the third stage of labor has too long been regarded as a normal accompaniment of parturition. Physicians have been taught that pregnancy fortifies the patient against an excessive blood loss by an increased blood volume. Dieckmann and Wegner and a host of other investigators have pointed out the fact that this increased blood volume is largely the result of a blood dilution, so that the cellular and hemoglobin content per unit volume of blood is actually less at the time of labor than at the onset of pregnancy. The vital

blood constituents in a serious hemorrhage are the blood cells and their oxygen carrying hemoglobin. Thus, this apparent safeguard against excessive bleeding is in reality a deception. During the first part of pregnancy there usually occurs a diminution in blood volume and blood constituents, often resulting in a real anemia. Should labor intervene at this period and be accompanied by a serious blood loss, the hazards of excessive bleeding would be increased.

Thus, in the prophylaxis of puerperal hemorrhage, accurate knowledge of the blood state is essential. Every pregnant woman must have a blood examination to determine early in the prenatal period the hemoglobin and cellular content and again, ideally, just before labor. This is as essential a procedure as the now accepted routine tests for the presence of syphilis. If an anemia is present, the patient should be placed on suitable therapy. It may even be necessary to resort to blood transfusions in marked anemias discovered late in pregnancy. Present day practice emphasizes prevention rather than cure and in no other field is this principle so important as in obstetrics.

There can be no sharp line between a normal and an abnormal blood loss. Although the average blood loss during the third stage of labor is approximately 300 c.c., wide variations occur. Usually a blood loss of over 500 c.c. is considered pathologic and is classified as a postpartum hemorrhage. The amount of blood loss which will provoke symptoms in one patient may produce little change in another. The size of the individual, the state of her blood,

\* From the Department of Obstetrics and Gynecology, the University of Chicago and the Chicago Lying-in Hospital.

her physical condition, particularly the presence of dehydration, all influence the hazards of an unusual blood loss. Pastore suggested that the blood loss be estimated in relation to the body weight and thus, indirectly, to the blood volume. A blood loss of more than 1 per cent of the body weight would comprise a postpartum hemorrhage: i.e., 600 c.c. in the patient who weighs 60 Kg. The determination of hemoglobin and cell volume provides an even more accurate evaluation of the blood loss. These measures may not be possible in the general practice of obstetrics, but they do emphasize the importance of an accurate measurement of the blood lost at the time of delivery and the importance of maintaining this blood loss at a minimum.

#### INCIDENCE

The frequency of postpartum hemorrhage varies considerably. It occurs less often in women who are delivered naturally, with little or no analgesia or anesthesia. Tucker and Benaron reported an incidence of 4.2 per cent in the home delivery service of the Maternity Center where 79 per cent of the deliveries are conducted without pain-relieving drugs of any kind. In contrast to these figures Peckham and Kuder reported an incidence of 6.14 per cent at the Johns Hopkins Hospital and Pastore 6.4 per cent at the New York Lying-in Hospital.

Many factors influence the likelihood of abnormal postpartum bleeding. Analgesia and anesthesia increase the hazards of the third stage by their effect on uterine tone and motility. Deep anesthesia may cause marked uterine relaxation, interfering with the normal mechanism for the control of bleeding in the third stage. The almost routine use of sedatives and anesthesia in hospital practice necessitates the use of oxytocic drugs to combat their effects during the third stage of labor. Overdistention of the uterus may increase the postpartum blood loss. This excessive distention may be due to an excessively large baby, a multiple pregnancy, or an abnormal ac-

cumulation of liquor amnii. There is a definite relationship between the length of labor and the frequency of postpartum hemorrhage. Pathologically long labors increase the incidence of abnormal bleeding. Unusual operative interventions such as version and extraction, difficult forceps delivery, or operations on the cervix tend to increase the blood loss. Special precautions should be taken in any of these conditions in which there is a tendency to an abnormal blood loss so as to decrease the danger of hemorrhage.

Improper conduct of the third stage of labor is the most common cause of an unusual blood loss during this period. The failure to recognize complete placental separation may lead to premature attempts at the expulsion of the placenta with a greatly increased blood loss. Delay in the expression of the placenta from the lower uterine segment may result in continued bleeding behind it. Unintelligent manipulation of the uterus during the third stage of labor increases the incidence of a pathologic third stage and its concomitant increased loss of blood.

#### THE THIRD STAGE OF LABOR

The proper appreciation of the mechanism and conduct of the third stage of labor is essential in the prevention of an abnormal blood loss. Recent contributions have clarified our understanding of this important phase of parturition. The proper conduct of the third stage must take into consideration its mechanism.

The placenta remains firmly attached to the uterine wall during the first and second stages of labor. The surface area of the placental site is approximately that of the placenta. (Fig. 1.) On the evacuation of the uterus, the uterine cavity is greatly reduced in size. This reduction is the result of contraction of the uterine wall so that it increases several times in thickness. This sudden decrease in the size of the uterine cavity results in a concomitant reduction of the surface area of the placental site. (Fig. 2.) This reduction takes place equally,



by a shrinking of the entire area rather than by a closing in of the periphery of this area. The placenta is a rather rigid organ

stage is largely due to the phase of expulsion, for the phase of separation is completed very rapidly.

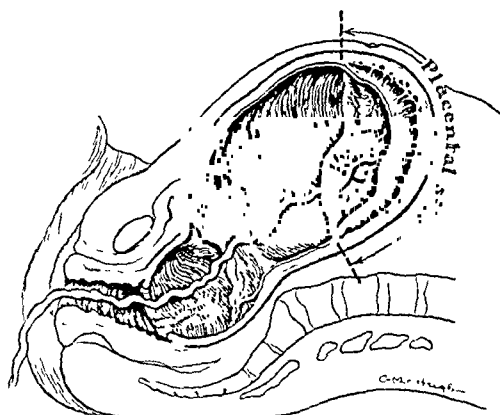


FIG. 1. Shows the normal uteroplacental relationships when the cavity of the uterus is distended with the fetus. Note the length of the placental site indicative of its surface area and the characteristic discoid shape to the uterus.

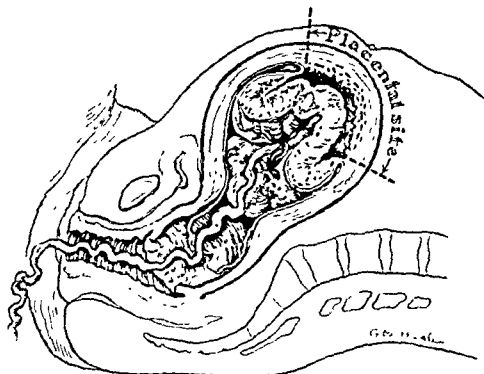


FIG. 2. Shows the uteroplacental relationships immediately after the baby has been expelled from the uterus and the placenta has separated from its uterine attachment. Note the great decrease in surface area of the placental site, the thickened uterine wall and the change in uterine contours.

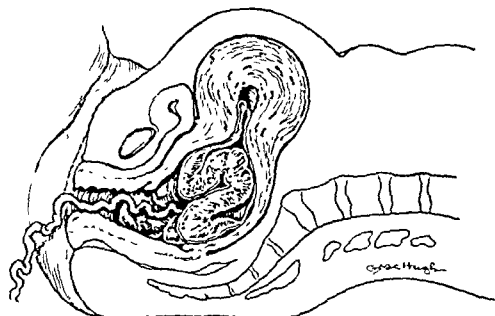


FIG. 3. Shows the uteroplacental relationships after the expulsion of the placenta into the lower segment and vagina. The fundus of the uterus has become globular and has risen; the lower segment is distended by separated placenta.

and does not contract with a diminution in its site of uterine attachment. This physical change must result in a shearing off or separation of the placenta in its vulnerable plane, the spongy decidua basalis. The more perfect this mechanism functions the more completely the placental separation will take place. The retroplacental clot is not necessary in the mechanism of separation. In most instances it accumulates as a result of an incomplete placental separation or after the placenta has separated from its attachment, while its expression from the lower uterine segment and vagina has been delayed. The time consumed by the third

The ideal conduct of the third stage consists of the recognition of placental separation and the immediate expression of the placenta after separation has taken place. The most reliable sign of placental separation is the change in the shape and position of the uterus. Immediately after delivery the organ can be palpated as a softened, discoid, pear-shaped body, the top of which reaches below the umbilicus. Immediately after separation of the placenta, the globular contracted corpus can be palpated at the level of the umbilicus, the softened lower uterine segment distended by the separated placenta above the symphysis. (Fig. 3.) The rise of the uterus in the abdomen is the result of the placenta being pushed out of the corpus and into the lower segment. Other signs of separation can be noted, but they are less valuable. The cord outside the vagina advances and a gush of blood may occur at this time.

In the expression of the placenta, several safeguards must be exercised. The corpus must be in a contracted state before expression begins. The entire uterus must not be pushed downward into the pelvis because this dislodgement favors excessive bleeding. The venous return is shut off and

the uterine sinuses become overfilled with blood, thereby tending to increase the blood loss. Pastore has suggested a method to prevent this undesirable complication, but the method is not applicable when the attendant is conducting the labor without help. The left hand is placed flat on the abdomen with the fingers directed under the symphysis, thereby preventing the uterus from entering the pelvis while the right hand expresses the placenta. The same end can be accomplished by the accoucheur if he will make pressure with the fingers of the left hand just above the symphysis while the right hand pushes down on the corpus. When the placenta is visible at the introitus, slight traction on the cord will deliver it most easily. However, traction on the cord is to be seriously condemned, for such manipulation on an incarcerated or partially adherent placenta may result in inversion of the uterus.

An oxytocic drug should be administered immediately after the expulsion of the placenta. Ergonovine 0.2 mg. intramuscularly is the most effective drug because of its prolonged action. In the service of the Chicago Lying-in Hospital it has almost entirely replaced pituitary preparations. Pituitary extract or its oxytocic fraction, pitocin, can be given, but the action of this drug is so short that ergonovine should be given orally to maintain uterine tone.

Hospital practice with its increased use of analgesia, anesthesia, and the artificial termination of pregnancy has resulted in a change in the conduct of the third stage. In many institutions patients receive 1 c.c. of pituitary extract intramuscularly immediately on the birth of the baby. When the drug is administered by this route it probably does not act for at least six or seven minutes so that the phase of placental separation is not interfered with. The contraction of the uterus induced by the oxytocic drug produces a most favorable condition for the second phase, that of expression. The placenta can easily be expressed from the lower uterine segment and vagina, thereby limiting the bleeding

following placental separation and decreasing the length of the third stage. Rarely, perhaps one case in a hundred, the placenta becomes incarcerated in a contracted zone between the corpus and lower segment and its manual expression may be difficult or impossible. Should active bleeding take place it may be necessary to remove the placenta manually. This complication is of such rare occurrence that the management of the third stage as described is routine in many institutions. It is not advisable, however, for deliveries in the home.

#### NEW MANAGEMENT OF THE THIRD STAGE OF LABOR

During the past three years a new management of the third stage of labor has been under careful study at the Chicago Lying-in Hospital. This method has yielded such striking results in the freedom from third stage complications and in the diminution of the blood loss that it is deserving of careful consideration with a view toward its more extensive use. The results in some 5,000 cases and a comparable control series are being carefully analyzed at this time and will be published in the near future.

If the phase of placental separation is entirely a physical phenomenon and is the result of a sudden reduction of surface area of the placental site, then theoretically the more rapidly this reduction takes place, the more complete will be the placental separation. There should be less likelihood of portions of the placenta remaining attached and thus interfering with the third stage. To accomplish this immediate contraction of the uterus following the birth of the baby, 0.2 mg. of ergonovine (ergotrate H, Lilly) is given intravenously after the head is delivered and as the anterior shoulder is brought into view. If one allows twenty to thirty seconds at this point for the drug to exert its action, the baby can then be delivered. The uterus contracts down almost instantaneously, separating the placenta cleanly from its attachment and pushing it out into the lower uterine

segment and vagina. Palpation of the corpus will reveal it to be globular and firm. The placenta can now be expressed from the vagina. This management of the third stage interferes with the phase of separation, whereas an oxytocic drug administered intramuscularly after the baby is born prepares the way for a more favorable phase of expulsion.

The advantages of the method described lie chiefly in the marked reduction in the loss of blood, and the freedom from complications of the third stage and the associated postpartum hemorrhage. The method has proved so effective on our service that the incidence of serious postpartum hemorrhage has become greatly reduced—so much so that the house staff is losing its dexterity in the treatment of this complication. The régime described is only applicable to institutional practice, for it requires someone to give the drug intravenously at the right time. Proper timing in the administration of intravenous ergonovine is essential. There have occurred a few instances of incarceration of the placenta in the contracted zone but this complication is not troublesome in an institution. The method should have a particular appeal in patients who are predisposed to abnormal uterine bleeding by a previous occurrence of postpartum hemorrhage, an excessively distended uterus, a long labor, or difficult operative interventions.

#### POSTPARTUM HEMORRHAGE

The usual causes of postpartum bleeding are abnormalities of the third stage of labor, uterine atony, and trauma of the reproductive tract. These conditions can be differentiated without difficulty and treatment must be directed to the cause of the hemorrhage. Intelligent management of the patient will do the most in conserving the patient's blood.

Postpartum hemorrhage most frequently results from incomplete separation of the placenta or delay in expression of the completely separated placenta. Premature attempts at placental expression may

result in only partial detachment and the typical Duncan mechanism is more likely to separate incompletely. If there is little or no bleeding, no interference is necessary and complete separation should be awaited, careful palpation of the corpus revealing when the placenta has been detached. In hospital practice it is customary to wait as long as an hour in the absence of bleeding. At the end of this time or in the event of frank bleeding, the placenta should be removed from the uterus. Crede's expression should be tried first in an attempt to complete the placental separation and expulsion. The contracted corpus is grasped in such a way that the uterus can be squeezed and pushed downwards at the same time. The uterus must not be pushed forcefully into the pelvis, for this may accentuate rather than diminish the hemorrhage. If moderate attempts at Crede's expression fail to deliver the placenta, manual removal should be employed.

Delay in the expulsion of the separated placenta from the lower uterine segment and vagina will increase the blood loss. The blood accumulates behind the placenta and the clots slowly distend the corpus cavity. This interferes with the uterine contractility, leading to atony and more bleeding. In the proper conduct of the third stage of labor it is important to recognize complete placental separation. While it is inadvisable to interfere with the phase of separation except in case of abnormal bleeding, it is necessary promptly to express the completely separated placenta to maintain the blood loss at a minimum.

Manual removal of the placenta is not an innocuous procedure. Nevertheless, the common feeling is that its dangers have been so well emphasized that the practitioner often delays this procedure at the expense of a serious blood loss. A considerable hazard of infection exists in the invasion of the uterus, but there is even greater danger in delay and continued blood loss. There is a direct relationship between the amount of blood lost and the incidence and severity of subsequent puerperal infection.

Rather than place too great emphasis on the danger of manual removal of the placenta, greater emphasis should be placed on the need of the most scrupulous technique in carrying out this procedure. The accoucheur should cleanse the patient very carefully, draw on a new pair of sterile gloves, and enter the vaginal orifice without contamination. If the placenta is simply incarcerated in the lower uterine segment, it can be removed by grasping it firmly. If a portion of its surface is still attached in the corpus cavity, this part must be separated before the placenta is removed. In the separation of a placenta still attached to the uterine wall, great care should be taken not to traumatize the wall. The entire placenta must be freed before an attempt is made to withdraw it from the uterus. If possible, 0.2 mg. of ergonovine should be given intravenously as the hand is withdrawn. The entire manipulation should be carried out at a single invasion of the reproductive tract. Repeated invasions increase greatly the hazards of infection. It is rarely necessary to resort to uterine tamponade.

Birth trauma as a cause of bleeding can usually be recognized without difficulty. At times, however, a patient may be treated for uterine atony, although this apparent atony is secondary to bleeding from some laceration. The following case is typical of this complication:

A patient was delivered by means of low forceps. The third stage was uneventful except that there occurred a steady trickle of blood during the repair of the episiotomy. The uterus remained firmly contracted. During the following twelve hours the uterus became distended with blood clots on three occasions. The house officer expressed the clots each time by pressure on the fundus and administered an additional oxytocic drug. When the accumulated blood loss became alarming, the patient was carefully examined and blood could be seen spurting from a tear lateral to the clitoris. What had happened was that the blood ran back into the vagina and the uterus. The clots interfered with the normal mechanism to maintain good uterine tone so that the uterus

gradually relaxed and became filled with clotted blood. This case history should emphasize the fact that the failure of a good oxytocic drug to maintain uterine tone is significant and a search for other causes of bleeding should be instituted promptly.

Hemorrhage from lacerations and trauma usually manifests itself immediately after the delivery of the baby and before the expulsion of the placenta. It will continue and become more marked after the placenta is out of the vagina. The amount of bleeding will vary with the extent of the trauma. Varicosities that have been cut or torn may cause a sudden profuse and serious blood loss. A small tear in the region of the clitoris can produce a small but long continued blood loss. The slow trickle is more serious than the sudden flooding because the latter excites immediate attention and the flow is stanching while the former may go unrecognized until the total blood loss has become formidable.

Bleeding from an episiotomy incision can be controlled by pressure until the cut tissues can be approximated. Constant pressure should be maintained during the repair because continued bleeding from this source may mount up to an appreciable volume in a short time. Although it is rarely advisable to clamp bleeders in an episiotomy wound, it may become necessary to approximate rapidly the bleeding surfaces before an orderly repair can be undertaken.

Lacerations in the vagina can usually be approximated by interrupted sutures. Ragged, extensive circular tears in the vault may be difficult to visualize. The torn edges should be united as far up as possible and the top suture can be used as a tractor to bring the uppermost portion of the laceration into view. Varicosities of the vagina may be difficult to obliterate. When pressure is removed, the field becomes so flooded that bleeding areas cannot be visualized. It is well to obtain as complete hemostasis as is possible and, if necessary, to resort to a tight vaginal pack. This can

be left in situ for twelve to eighteen hours, after which it can be safely removed. Before placing the pack, one should make

*Placenta Previa.* The placental attachment in the lower uterine segment provides an abnormal mechanism for the third stage

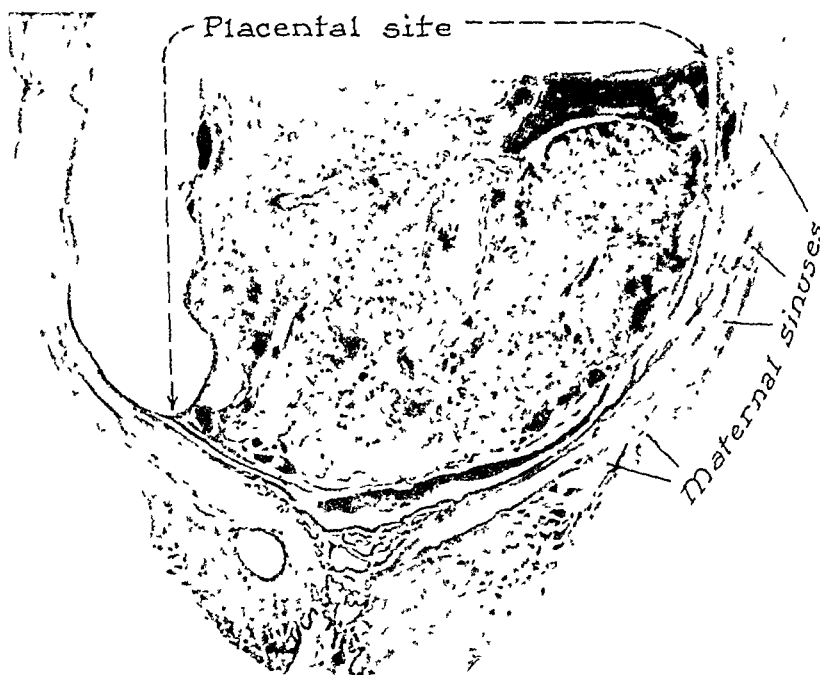


FIG. 4. Histologic preparation of the lower uterine segment and attached placenta in a case of placenta previa. The wall of the lower uterine segment is markedly vascularized by the numerous sinuses of the placental site, thereby altering its normal integrity and making it more vulnerable to trauma. The proximity of the placental site to the cervix increases the hazards of infection.

certain that all the bleeding is the result of vaginal varicosities and none of the hemorrhage is of uterine origin.

Lacerations of the cervix can usually be brought into view by the use of ring forceps which will not traumatize the cervix. The cut or torn surfaces can be approximated by interrupted chromicized sutures. It is important to obtain good exposure. The uppermost stitch should approximate the very top of the laceration so as to obliterate a torn vessel which can retract into the musculature. The repair should be completed rapidly, for prolonged traction on the uterus may result in uterine venous engorgement and bleeding from this source.

There are certain complications incidental and accidental to pregnancy in which hemorrhage is a major factor. The conduct of the third stage of labor in these conditions deserves special consideration.

of labor. The placental site in this abnormal location does not have sufficient musculature to undergo the same degree of contraction as in the usual location. This lack of musculature interferes with normal contraction and retraction of muscle fibers and bundles and diminishes the value of this mechanism in the constriction of the maternal sinuses of the placental site. (Fig. 4.) Lastly, the lack of a normal decidual buffer zone in the lower uterine wall results in an abnormal placental attachment and an absence of the usual plane of cleavage, further complicating the third stage.

The third stage may be allowed to proceed normally if there is no abnormal bleeding. As soon as separation of the placenta has taken place, it should be expressed in the manner previously described. The patient should then be given

an oxytocic drug, preferably ergonovine intravenously. If bleeding follows the delivery of the baby, prompt preparation

One final word of caution must be added. Statistics indicate that as many woman die of infection following placenta previa as of



FIG. 5. This uterus was removed at autopsy from a patient with puerperal infection. Note the retained placental cotyledon in the corpus cavity which first resulted in postpartum hemorrhage from uterine atony and subsequently was the focus of a fatal thrombophlebitis.

should be made for the exploration of the lower uterine segment and the manual removal of the placenta. The placenta must be carefully separated before it is removed. A careful examination of the cervix and lower segment must be made to determine if any trauma has occurred. It must be emphasized that the lower uterine segment in the presence of placental attachment becomes pathologically vascularized and is subject to extensive trauma even with minor manipulations. Any such trauma should be repaired. If bleeding cannot be controlled by suture, it may be necessary to exert pressure against the maternal sinuses in the lower uterine segment by means of tamponade. If only the lower uterine segment is packed, the tampon may serve as a plug concealing bleeding which continues above it. In a rare instance such tamponade may not effectively control the continued hemorrhage in which case preparations for immediate hysterectomy should be made. A rapid operation may save the life of a patient who would otherwise have succumbed.

the hemorrhage associated with this condition. The close proximity of the uterine sinuses to the vagina and to sources of infection increases the hazards of all manipulations. Extreme care must be exercised in the management of a patient with placenta previa to decrease the hazards of infections.

*Abruptio Placentae.* Premature detachment of the normally implanted placenta is associated with profuse hemorrhage during the labor and particularly the postpartum period. The hemorrhage may be so overwhelming in amount that the patient is completely exsanguinated within a short time. The control of excessive blood loss in this complication involves the entire management of the condition. The blood may accumulate as a huge retroplacental hematoma, gradually distending the uterus and be almost entirely concealed. Blood may extravasate into the uterine wall between the leaves of the broad ligaments, retroperitoneally, to involve almost the entire pelvis. The separation of the placenta is usually completed or partially completed

at the onset of the accident. The placenta can usually be expressed without difficulty, but the atony of the uterus at this period is the serious problem. A careful removal of all the clots and the intravenous administration of ergonovine should result in good uterine tone providing the uterine myometrium has not been too extensively disorganized by hemorrhagic infiltration. If the uterus fails to maintain good uterine tone, tamponade can be carried out, packing the entire reproductive tract as firmly as possible. Since the advent of the powerful and rapid acting oxytocic agent, ergonovine, we have been impressed with the fact that if bleeding cannot be controlled by this drug, the uterine musculature is probably seriously impaired and hysterectomy should be carried out with all possible speed. Uterine tamponade in these desperate cases only masks the picture and delays the institution of more effective therapy. Timely transfusion of effective amounts of blood is life-saving in these late hemorrhages of pregnancy.

*Retained Placental Tissue.* In the prophylaxis of postpartum hemorrhage the careful examination of the placenta is most important. This is a responsibility which the accoucheur should not relegate to some other individual. Retained placental fragments or entire cotyledons lead to uterine atony and its concomitant hemorrhage and even more important, they predispose to puerperal infection. (Fig. 5.) If a fragment of placenta is missing, it should be promptly removed. Needless to say, there is danger in the invasion of the puerperal uterus, but with a careful technique, this procedure need not increase the hazards of the patient. The placental tissue can usually be found and peeled off the uterine wall. Membranes left in the uterine cavity rarely cause trouble and are usually passed in the lochial discharges during the first days of the puerperium.

*Neoplasms of the Uterus.* Fibromyomata of the uterus occasionally complicate the third stage of labor. These tumors may interfere with normal separation of the

placenta or with the normal contractility of the myometrium. Although the third stage is usually uneventful, the attendant should anticipate a pathologic third stage and be prepared to meet it. If the placenta fails to separate completely and bleeding intervenes, manual removal may be resorted to. Rarely, a submucous fibroid nodule may cause the abnormal placental attachment. Intravenous oxytocic drugs should maintain good uterine tone, but it may become necessary to tampon the reproductive tract.

*Placenta accreta* is a very rare complication that may not occur once in 20,000 births. A poor or an absent decidual development results in an invasion of the myometrium by chorionic villi and the absence of the usual plane of cleavage between placenta and uterine wall. This abnormal attachment may involve a small localized portion of the placenta or the greater part of its surface. Manual removal of such an abnormally adherent placenta is impossible. Hysterectomy is the procedure of choice when this condition is recognized.

*Inversion of the uterus* is a rare complication which results from improper conduct of the third stage. It has not occurred in over 50,000 births at the Chicago Lying-in Hospital. The usual mechanism of production is traction on the cord of the attached placenta when the uterus is in an atonic state. Immediate replacement of the uterus is indicated, following which an oxytocic drug will usually maintain normal relationships. Where the uterus has been inverted for some little time, it usually is necessary to resort to surgical correction. This accident is usually associated with profuse hemorrhage.

*Rupture of the uterus* may occur during the delivery and produce alarming third-stage bleeding. Immediately after difficult operative interventions a careful exploration of the lower uterine segment and corpus cavity should be made. The rupture can usually be palpated. It may be incomplete and only involve the lower uterine segment in which case repair from below

may be possible. Uterine tamponade may help to control the bleeding more securely. Usually, it is safer to resort to immediate hysterectomy. The operation should be carried sufficiently low so as to include careful ligation of the uterine vessels on both sides.

Rare blood dyscrasias may predispose to excessive bleeding in the third stage. A careful history will usually elicit data concerning the blood deficiency in which event careful blood studies should be made during pregnancy. This is the only condition in which whole blood should be used in any transfusion rather than the usual citrated blood.

#### PARENTERAL FLUIDS AND BLOOD TRANSFUSION

It cannot be too strongly emphasized that measures for combating blood loss are a most essential part of any treatment of hemorrhage in pregnancy. The subsequent maternal mortality, serious puerperal infection, and prolonged convalescence and invalidism can be greatly reduced by a serious attempt to restore in some measure the blood loss of the patient. For maintaining blood volume, saline or Ringer's solution can be given by hypodermoclysis, using 16 gauge needles. Glucose solution in 20 per cent concentration should be given intravenously at as slow a rate as possible, discontinuing its administration just as soon as blood is available. No more than 500 c.c. should be given unless a liberal blood transfusion follows. It must be remembered that large amounts of hypertonic glucose solution draw liberally on the fluids in the tissues and increase blood coagulation time. Although the blood volume be restored, sufficient circulating hemoglobin must be present to carry on the vital functions of life. The amount of the transfusions should depend on the blood loss, averaging 500 to 800 c.c. in the usual case. Citrated blood is as efficacious as whole blood and can be given easily. Suitable donors must be selected with the greatest care.

The use of acacia as an emergency measure has been advocated. In spite of its appeal because of its ready availability, serious and fatal accidents have been reported. Its use should be entirely discontinued or very guarded.

Blood banks are becoming more numerous so that in time stored blood may be more readily available. At the present time such blood can be obtained only at larger medical centers.

#### REFERENCES

1. BUXBAUM, H., and UDESKY, I. C. *Illinois M. J.*, 70: 428, 1936.
2. CALKINS, L. A. *Am. J. Obst. & Gynec.*, 29: 231, 1935.
3. CALKINS, L. A. *J. A. M. A.*, 101: 1128, 1933.
4. DAVIN, E. J., SPIELMAN, F., and ROSEN, J. A. *Am. J. Obst. & Gynec.*, 33: 463, 1937.
5. DAVIS, M. E. *J. A. M. A.*, 109: 1631, 1937.
6. DAVIS, M. E. *Am. J. Obst. & Gynec.*, 32: 518, 1936.
7. DAVIS, M. E. *S. Clin. North America*, 15: 737, 1935.
8. DAVIS, M. E., ADAIR, F. L., CHEN, K. K., and SWANSON, E. E. *J. Pharmacol. & Exper. Therap.*, 54: 398, 1935.
9. DAVIS, M. E., ADAIR, F. L., and PEARL, S. J. A. *M. A.*, 107: 261, 1936.
10. DAVIS, M. E., ADAIR, F. L., ROGERS, G., KHARASCH, M. S., and LEGAULT, R. E. *Am. J. Obst. & Gynec.*, 29: 155, 1935.
11. DAVIS, M. E., and MCGEE, W. B. *Surg., Gynec. & Obst.*, 53: 768, 1931.
12. DIECKMANN, W. J., and DAILY, E. F. *Am. J. Obst. & Gynec.*, 30: 1, 1935.
13. DIECKMANN, W. J., and WEGNER, C. R. *Arch. Int. Med.*, 53: 345, 1934.
14. DOUGLASS, L. H. *South. M. J.*, 30: 639, 1937.
15. DEPUY, C. A. *California & West. Med.*, 47: 233, 1937.
16. ELDER, J. H. *Am. J. Obst. & Gynec.*, 37: 327, 1939.
17. FORTIN, F. F. *Am. J. Obst. & Gynec.*, 35: 761, 1938.
18. HAUCH, E., and MOLLER-CHRISTENSEN, E. J. *Obst. & Gynaec. Brit. Emp.*, 43: 1145, 1936.
19. HUNTER, W. *Post-Grad. M. J.*, 13: 419, 1937.
20. KITCHEN, D. K. *Tri-State M. J.*, 8: 1563, 1935.
21. LAIRD, T. *Lancet*, 2: 998, 1938.
22. MOIR, C. *Proc. Roy. Soc. Med.*, 28: 1654, 1935.
23. PAGE, C. W. *West. J. Surg.*, 44: 346, 1936.
24. PASTORE, J. B. *Am. J. Obst. & Gynec.*, 31: 78, 1936.
25. PASTORE, J. B. *Am. J. Obst. & Gynec.*, 32: 859, 1936.
26. PASTORE, J. B. *Am. J. Surg.*, 35: 417, 1937.
27. PECKHAM, C. H., and KUDER, K. *Am. J. Obst. & Gynec.*, 26: 361, 1933.
28. RANDALL, L. M. *M. Clin. North America*, 22: 1197, 1938.
29. RAWSON, W. F. *Brit. M. J.*, 1: 1317, 1935.
30. RUCH, W. A. *Mississippi Doctor*, 12: 62, 1937.
31. SALACZ, P. J. *Obst. & Gynaec. Brit. Emp.*, 42: 476, 1935.
32. STANDER, H. J. In *Williams Obstetrics*. New York, 1936. Appleton.
33. TUCKER, B. E., and BENARON, H. B. *W. M. Clin. North America*, 22: 197, 1938.
34. WILLIAMS, N. H. *West J. Surg.*, 47: 223, 1939.



# PUERPERAL INFECTION\*

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**P**UERPERAL infection results when the female generative tract has a lowered resistance to the organisms which invade it during or following delivery or abortion; or when the virulence of the invading organism is unusually great. Of course, both conditions may be present in the same patient. Intrapartum infection is probably much more frequent than is generally believed and can only be prevented by early prophylaxis.

Contamination of the genital tract may be either (1) endogenous, due to organisms harbored by the vagina; or (2) exogenous, due to organisms introduced from without. Prevention of the first type of infection is possible if prophylaxis is started early enough in labor. The latter type of infection must be controlled by preventing the introduction of organisms from without by proper surgical technique—asepsis, antisepsis, proper masking and conservative obstetrical intervention.

A résumé of the findings which have been made since our study of puerperal infection was begun in July, 1924, may be helpful to those who encounter this disease with its various manifestations.

In the report of the Children's Bureau,<sup>1</sup> puerperal septicemia was given as "the most important cause of death connected with pregnancy and childbirth. It caused 40 per cent of the 7,380 deaths included in the study." A later report for 1937 stated infection to be the cause of death in 35 per cent of cases. Sepsis has maintained a relatively level curve from 1915 to 1937<sup>2</sup> as a factor in maternal mortality in the United States. Deaths assigned to this cause have ranged from 24 to 18 per 10,000 live births during this period. Such reports make us realize the great importance of puerperal

infection as a stumbling block in our attempts to lower the high maternal mortality rate of the United States as compared with certain foreign countries.

Another point brought out in the report is that infection, in the fatal cases, developed in the hospital in but 15 per cent. This seems to counteract the general impression that most cases of infection develop in hospitals, probably because of too great a tendency to interfere with the course of labor or abortion.

The observations of Schottmüller<sup>3</sup> led Drs. O. H. Schwarz and W. J. Dieckmann<sup>4,5</sup> to investigate the bacteriology of the cases on our service and they soon confirmed his findings. The most important point was that a group of anaerobic streptococci which had been overlooked or considered only as nonpathogenic saprophytes were really accountable for a very large percentage of cases of puerperal infection.

In a series of 246 cases<sup>6</sup> of puerperal infection treated on the Obstetrical and Gynecological Service of Washington University, anaerobic organisms were isolated from the uterus in 84.1 per cent. The number of deaths was thirty-one and analysis of causes is shown in Table 1.

TABLE 1

		Type (Colebrook)
Peritonitis.....	16	III
Septicemia.....	10	IV
Thrombophlebitis.....	4	II
Pelvic abscess (ruptured).....	1	II
	—	
	31	

If these cases are classified on the clinicopathologic basis of Colebrook,<sup>7</sup> a very important point is emphasized—namely that peritonitis is probably the most serious complication of all. Septicemia may re-

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spond to various types of therapy, but when a true peritonitis develops the prognosis is most guarded.

Schottmüller stressed the relationship between thrombophlebitis and the anaerobic streptococci. We observed the same finding in our series and lost four out of fifteen over a period of five and one-half years. Since January, 1930, we have not had such a death. This is probably due to two main factors (1) prophylaxis and (2) early active treatment of uterine infections. Of late we observe only an occasional mild case of thrombophlebitis.

As stated above, we have had thirty-one deaths due to puerperal infection. Upon further analysis it is brought to our attention that thirteen of these deaths occurred among patients delivered by our service, eight of which were delivered by cesarean section.

TABLE II

TYPES OF ORGANISMS IN THIRTY-ONE FATAL CASES		
Anaerobic streptococcus	15	(4)
Hemolytic streptococcus	7	(2)
Staphylococcus albus	7	(6)
Streptococcus viridans	1	(0)
Nonhemolytic streptococcus	1	(1)
	<hr/> 31	<hr/> (13)

The incidence of infections due to *Staphylococcus albus* was found to be due to faulty technique in the sterilization of gloves and was soon corrected. Note the important rôle played by the anaerobic streptococcus in these fatal cases whether delivered in the hospital or outside.

Upon noticing the importance of infection as the cause of mortality following cesarean section, we undertook the study of the bacteriology of the uterus at the time of operation and correlated the findings with the use of antiseptic vaginal instillations. The antiseptic used was 1 per cent neutral acriflavine in glycerin, as described in a recent article.<sup>8</sup> The instillation is best given with an asepto syringe No. 2042. This syringe holds 8 c.c. (average dose) and is rubber tipped so that it can do no serious damage. An instillation is given upon admission and repeated every four hours if

the patient is in active labor. In waiting cases at or near term and cases which may be delivered by section, instillations are ordered given once daily unless the membranes have been ruptured when instillations are given twice daily.

As a control group for this study we refer to the report of Harris and Brown<sup>9</sup> in which cultures were obtained in the same way, but no instillations were used. The contrast is very marked. In their study of fifty patients, uterine culture was positive in 44 per cent. They noted the predominance of anaerobic streptococci. Anaerobic growth was obtained in 45 per cent of the positive cultures. "No sterile cultures were obtained from patients in whom active labor had lasted for six hours or more and only one positive culture was obtained where labor had progressed less than six hours. . . . when cesarean section is definitely indicated the ideal time for its performance is at an appointed time at the end of pregnancy or at the very beginning of labor." Later in labor they suggest employment of the low cervical section or the radical procedure (supravaginal hysterectomy).

In a series of 144 cases studied at the St. Louis Maternity Hospital, the incidence of positive uterine culture was 4.1 per cent when vaginal instillations of acriflavine were employed. Anaerobic growth was present in 83 per cent of the positive cultures. Intrapartum infection accounted for 50 per cent of the positive cultures. A negative uterine culture was obtained as late in labor as 107½ hours with the use of instillations. In two cases forceps delivery was attempted before section was performed and the uterine cultures were negative. Since 1931, puerperal infection as the cause of mortality associated with cesarean section, has been eliminated, apparently due to the use of antiseptic vaginal instillations. The indication for the radical procedure of supravaginal hysterectomy because of infection has been avoided. This technique makes it relatively safe to postpone section until a much later hour in the labor

than has been recommended by other reports.

In the report on Maternal Deaths,<sup>1</sup> abortion was reported in 45 per cent of the deaths due to septicemia. The report for 1937<sup>10</sup> mentioned this proportion as 40 per cent. In the study of uterine cultures in approximately 1600 abortion cases, 60 per cent were found to be positive. Anaerobic growth was obtained in 92 per cent of the positive cultures. This again emphasizes the importance of this group of organisms in puerperal infection. Contrast this with the lower incidence of the hemolytic streptococcus, which was found in 7.2 per cent of a series of 2,042 uterine cultures.

The importance of the hemolytic streptococcus is not to be belittled for a moment when it is present and causing the disease. In the twenty deaths which occurred in a series of approximately 1600 abortions on the service of St. Louis City Hospital No. 1 between 1934 and 1939,<sup>11</sup> (to be reported) 35 per cent showed hemolytic streptococcus present in the uterine cultures and 25 per cent in the blood cultures (mortality 1.2 per cent).

In view of our results,<sup>12</sup> it seems advisable to continue the active gentle treatment of the uterine cavity, as early as possible in cases of suspected uterine contamination: (1) to obtain the diagnosis; (2) to determine the type of organism present; (3) to arrest blood loss; (4) to shorten convalescence; and (5) to avoid complications. Do not use a sharp curette in the treatment of such cases.

Posterior colpotomy is of great value in the treatment of patients who develop pelvic infections that finally point in the cul-de-sac. A word of caution should be given in regard to the handling of such cases: Wait until the process is well localized. If possible, avoid the use of general anesthesia during the procedure for fear too much force may be used and result in the rupture of such an abscess into the peritoneal cavity as has occurred in a few instances. Place a good sized T tube and allow it to remain in place long enough

(usually six weeks). Such a tube should be cut spirally in order to avoid too much pressure against the vaginal wall with resultant erosion and possible perforation of the rectum.

Prevention of maternal mortality from infection will result from: (1) thorough surgical preparation of patient; (2) excellent aseptic technique; (3) proper use of masks; (4) antiseptic vaginal instillations; (5) prompt isolation of infected patients; (6) early gentle evacuation of uterine debris and establishment of adequate drainage; (7) transfusions as indicated; (8) chemotherapy when indicated.

Without the assistance of chemotherapy the maternal mortality from puerperal infection on the Obstetrical Service of Washington University has been:

	Deliveries	Deaths
July, 1924-Jan. 1932.....	9,529	13
Jan. 1932-Jan. 1940*.....	12,913	0

\* Vaginal instillations used during this period.

These results coincide with the statement of Schottmüller: "Heute muss es also heissen: Die Gefahr kommt weniger von Aussen als von Innen."

#### TREATMENT

The use of vaccines is too slow to be of value. Intravenous dyes have proved of little use. Antitoxin helps in the treatment of specific organisms, but passive immunity with antiserum has never appealed to me. Nonspecific therapy does not seem to be indicated in acute infections. Heat may be of benefit later in the course of the disease when the patient's temperature has approached normal. After the febrile period is over many patients are found to be in need of thyroid medication due to depletion of the thyroid.

Transfusion is probably the best therapeutic agent we have available. One should be guided by the hemoglobin level and try to maintain it between 90 and 100

per cent. The anaerobic streptococcus causes marked anemia due to its proteolytic action on red cells and frequent transfusions of from 500 to 750 c.c. seem to give best results. Immunotransfusion is of value if proper donors are available.

Chemotherapy with drugs of the sulfanilamide group should not be used indiscriminately because of the possible by-effects which make the patient feel miserable and may inhibit her recovery. They also frequently mislead the physician into the belief that the patient is much worse off than she really is. When the bacteriologic findings in a given case indicate that this group of drugs might be of value, one may proceed cautiously with close observation, using the least toxic preparation available and giving moderate doses over as short a period as possible. The results of such therapy are not 100 per cent good even in patients infected with the hemolytic streptococcus. It is necessary to follow closely the effect on the red blood cells, white blood cells and hemoglobin, and to check the level of the drug in the blood stream from time to time. There is no evidence of the value of this group of drugs in patients infected with anaerobic streptococci and since these organisms most frequently are the offenders in puerperal infection, it is wise to omit sulfanilamide medication until the hemolytic streptococcus is proved to be present. It seldom is present when the obstetrical care of patients is what it should be. Perhaps later we may have some related drug which will be of more general value.

The reports of Colebrook and Purdie,<sup>13</sup> Morris,<sup>14</sup> Chandler and Janeway,<sup>15</sup> and Waters,<sup>16</sup> suggest the value of sulfanilamide and allied drugs in the treatment of puerperal infection, but their results are not very convincing since similar results are obtained without such drugs.

When a patient in the puerperal state develops signs of infection, which cannot be accounted for after the usual diagnostic methods have ruled out all other possible infections, it seems justifiable to investigate

the uterine cavity. The surgical principles involved in our treatment of such cases are; (1) drainage of an infected wound site, and (2) debridement of a potentially infected cavity. This is done with a minimal amount of manipulation in order that further trauma may be avoided. We have demonstrated that this procedure can be safely performed by a junior intern under proper supervision. A general anesthetic is not used, because this would remove the inhibiting influence of the patient's response to pain which is usually indicative of two active manipulation. The patient should be under the influence of some sedative so that she is not too apprehensive. Morphia (.01 Gm.) with hyoscine hydrobromide (0.0005 Gm.) followed by hyoscine (0.0005 Gm.) in forty-five minutes is given, the second dose administered at least thirty minutes before the patient is prepared for examination.

The perineum is prepared with tincture of mercuric iodine. The bladder is *not* catheterized because of the danger of contamination which may frequently superimpose a urinary infection. Drapes are placed. A Graves' vaginal speculum is used to obtain exposure of the cervix. If this is not satisfactory, several vaginal retractors will be necessary. The vagina and cervix are then prepared with the above solution. The cervical canal is treated with the solution and dried carefully with sterile gauze. A culture is obtained from the uterine cavity with a modified Little tube. If it is not possible to have careful bacteriologic investigation of the material obtained, several smears can be made and stained by the Gram method. This has been done routinely and found to check very well with the bacteriologic findings. Both aerobic and anaerobic blood agar slants should be made. The Wright anaerobic technique is used in the search for anaerobic organisms.

After the culture has been obtained, a gentle bimanual examination is done to determine evidence of any spread of the uterine infection, pelvic abscess or thrombophlebitis. This is also done without an

anesthetic in order that the patient's reaction to pain may limit the extent of the examination. Too much pressure might cause rupture of an abscess internally. The uterine cavity is very carefully investigated with a Foerster's sponge-holding forceps, plain jaw. Dilatation of the cervix is usually sufficient to permit this. The closed sponge forceps is inserted to the depth desired, opened, closed, and removed to see if any tissue has fallen within the jaws. The forceps should not be advanced with the jaws open, because of the danger of grasping the uterine muscle. The uterine wall is next explored very systematically and with great gentleness by means of a "uterine wiper" (formerly called a vaginal depressor) much as a windshield wiper covers the glass of a windshield, without marring the surface. (No curettage is done.)

The uterus is usually found to be relaxed in such cases. After mechanical removal of any retained debris, the patient is given an intra-uterine douche, using a Bozeman's extra large intra-uterine douche nozzle. This instrument permits the free exit of the solution from the uterine cavity without positive pressure being established. Two liters of a 1:1000 solution of potassium permanganate in sterile water at 105 to 110°F. are used. This solution is usually acidulated with 50 c.c. N/1 sulfuric acid. The bottom of the douche can is held at the level of the symphysis so that the water pressure of the solution as it enters the douche nozzle is 15 cm. or less. Such a douche results in (1) removal of small bits of tissue remaining after mechanical emptying of the cavity; (2) firm contraction of the uterus, including the cervix, so that bleeding is controlled and the sinuses are closed; (3) elimination of the putrid discharge which is characteristic of anaerobic infections. It is seldom necessary to repeat the procedure.

## CONCLUSION

Puerperal infection in the early stage is primarily a surgical disease, infection of a wounded area (placental site), and should be treated accordingly. Drainage should be established early and maintained if necessary. All debris should be evacuated as gently as possible. Avenues for spread of infection should be closed by keeping the uterus well contracted. Complications are avoided by early treatment. Prophylaxis is accomplished by the early, consistent use of antiseptic vaginal instillations. These are of value in avoiding both endogenous and exogenous infection. Excellent aseptic technique with a minimum of interference by attendants will largely eliminate exogenous infection. Transfusion is of great value. Chemotherapy should be used when there is indication.

## REFERENCES

1. U. S. Department of Labor, Children's Bureau. Publication No. 221.
2. U. S. Department of Labor, Children's Bureau. Chart 7880.
3. SCHOTTMÜLLER. *Mitteil. a.d. Grenzgeb. d. Med. u. Chir.*, 21: 450, 1910.
4. SCHWARZ, O. H., and DIECKMANN, W. J. *South. M. J.*, 19: 370, 1926.
5. SCHWARZ, O. H., and DIECKMANN, W. J. *Am. J. Obst. & Gynec.*, 13: 467, 1927.
6. SCHWARZ, O. H., and BROWN, T. K. *Am. J. Obst. & Gynec.*, 31: 379, 1936.
7. COLEBROOK, L., and KENNY, M. *Lancet*, 2: 1319, 1936.
8. BROWN, T. K. *Am. J. Obst. & Gynec.*, 38: 969, 1939.
9. HARRIS, J. W., and BROWN, J. H. *Am. J. Obst. & Gynec.*, 23: 133, 1927.
10. U. S. Department of Labor, Children's Bureau. Chart 7987.
11. To be reported.
12. BROWN, T. K., and HUNT, G. A. *Am. J. Obst. & Gynec.*, 32: 804, 1936.
13. COLEBROOK, L., and PURDIE, A. W. *Lancet*, 2: 1237, 1291, 1937.
14. MORRIS, T. J. *Am. J. Obst. & Gynec.*, 38: 67, 1939.
15. CHANDLER, C. A., and JANEWAY, C. A. *Am. J. Obst. & Gynec.*, 38: 187, 1939.
16. WATERS, E. G. *Bull. N. Y. Acad. Med.*, 15: 597, 1939.



# RESPIRATORY COMPLICATIONS IN THE CARE OF THE NEWBORN\*

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THE establishment of respiration is the first concern as the child emerges from the intra-uterine environment and is surrounded by air instead of by the liquid in which he has been immersed for many months. The hazard of the transition which occurs abruptly at birth is illustrated by the frequency with which injury of the respiratory system is observed at the time of delivery, since it involves an experience in obstetric pathology which is inescapable.

The numerous complications of fetal life which result in failure to survive have recently been analyzed by Potter and Adair<sup>1</sup> in a series of 17,000 deliveries. The present discussion is concerned with the respiratory system, especially with reference to the origin and prevention of injuries before birth.

Injuries of the respiratory system which are evident at the time of birth include: (1) asphyxia, or failure of the nervous mechanism of respiration; (2) atelectasis, or incomplete dilatation of the pulmonary alveoli; and (3) pneumonia.

Despite the common occurrence of depression and failure of respiration in the newborn and the numerous reports of autopsy examinations of the lungs of still-born babies, there has persisted considerable obscurity regarding the pathogenesis of respiratory complications which are seen at the time of birth. Consequently, methods of dealing with asphyxia neonatorum and prevention of pulmonary damage have been largely empiric and controversy has been promoted in proportion to the variety of individual experience. It is evident that consideration of the prevention of respiratory injuries involves first of all demonstra-

tion of the pathogenesis of respiratory failure and of pulmonary damage.

Since these respiratory complications are immediately evident at the time of birth, it follows that the injuries originate during intra-uterine life. It is essential, therefore, to determine the normal state of activity of the respiratory system before birth in order to understand the mechanism by which abnormalities arise. Many difficulties attend the study of the fetus in the intact uterus before birth. It is a clinical observation that at the time of cesarean section the fetus is in a state of apnea, even though general anesthesia is eliminated and local infiltration or spinal anesthesia is used. Prolonged apnea has been regarded as the characteristic condition of the fetal respiratory system throughout embryonic life.<sup>2</sup> It has seemed logical that the entrance of amniotic fluid into the pulmonary alveoli must be abnormal and even result in drowning of the fetus at birth.

Experiment has thrown considerable light upon these problems. Under laboratory conditions the state of activity of the fetal respiratory system has been determined by direct observation of fetuses in the unopened uterus.<sup>3</sup> For instance, in rabbits in which labor has been inhibited following the addition of fresh lutein tissue in the ovaries, by the injection of extract of pregnancy urine, fetuses at full term or post mature development have been observed directly for many hours after the exposure of the uterus by laparotomy. Anesthetics were eliminated by section of the lumbar spinal cord prior to laparotomy. Observation of fetuses in the intact uterus

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under these conditions revealed striking activity of the respiratory organs in the intra-uterine environment. The respiratory movements continued for many hours at a constant level. When suitable experimental methods are employed, it is evident that the first respiration is not initiated at birth, but extends far back into embryonic life.

In the human as well as in other species, long periods of automatic activity of the fetal respiratory organs have been noted. In women the rhythmic fetal movements are transmitted through the abdominal wall and are integrated in a pattern that is characteristic of respiration. Records of the excursions of the abdominal wall have been obtained by kymograph and by motion pictures.<sup>4</sup>

In view of these findings regarding the normal physiologic activity of the respiratory organs before birth, it is evident that depression or failure of respiration at birth must be regarded as the suppression of previous activity rather than the failure of some new mechanism to begin functioning. The pathogenesis of asphyxia neonatorum is thus closely related to changes occurring in the intra-uterine environment. Control of asphyxia centers upon the period before birth.

The next step in the prevention of respiratory failure at birth involves recognition of the factors which cause apnea of the fetus within the uterus. If one turns to experiment in order to trace the development of the apneic state, starting with fetuses which show active respiratory movements, it is found that three main types of fetal apnea may be distinguished, namely, anoxemic, acapnic, and anesthetic. The normal regulation of fetal respiration depends upon the oxygen and carbon dioxide level of fetal blood, but differs in certain respects from that of the adult. Oxygen want depresses or abolishes fetal respiratory movements. Carbon dioxide deficit results in depression or apnea of the fetus, showing that a certain level of carbon dioxide is essential for the maintenance of fetal respiration. An excess

of carbon dioxide has little effect. The fetal respiratory system is peculiarly sensitive to narcosis. Respiratory movements may be abolished in the fetus at a level of analgesia which does not impair maternal respiration. Of the three factors found to be depressant to fetal respiration, anoxemia and anesthesia stand out preëminently.<sup>5</sup> Acapnic depression is so readily reversible that there is little evidence that acapnia has a significant rôle in the production of permanent injury. In current reports from various clinics regarding the relation of anoxemia and anesthetics to asphyxia neonatorum additional evidence is available for evaluation of the importance of these factors.<sup>6,7,8,9</sup>

While prevention of asphyxia is related to an appreciation of the etiologic factors which are involved, resuscitation of the apneic child remains a large problem. Marchetti<sup>10</sup> has recently presented a critical survey of methods and principles which have been tested in such emergency. In a series of studies upon the maintenance of artificial respiration, Murphy<sup>11</sup> showed the effectiveness of the Drinker respirator in keeping up pulmonary ventilation at a level which was adequate to support life for many hours during which time the infant promptly showed respiratory failure unless artificially aided. Murphy has also emphasized the aid to the thoracic circulation which respiratory excursions exert.

Regarding the usefulness of respiratory stimulants such as alpha-lobeline, coramine, caffeine, metrazol, and cyanide, it has been difficult to evaluate various reports concerning their rôle at the time of birth, since these drugs are administered usually following labor which is complicated by various factors that may alter respiratory activity, such as anoxemia, anesthesia, and trauma. In order to determine the effect of these respiratory stimulants upon the normal newborn, we<sup>12</sup> have carried out experiments upon newborn rabbits immediately following delivery. Results showed that response by increase in rate or depth of breathing was

brief, lasting less than a minute. There was a narrow margin between the dosage level at which stimulation appeared and the dosage at which convulsions or death occurred. Thus with lobeline, convulsions followed a dose which was twice the minimal effective amount. With caffeine, metrazol, coramine, and cyanide, convulsions followed a dose of three times the minimal effective amount. Furthermore, death frequently followed the onset of convulsions resulting from the administration of alpha-lobeline, caffeine or coramine.

The possibility of prevention of intra-uterine pneumonia is closely related to the nature of the etiologic factors which are concerned. Outstanding among the factors which are involved is contamination of the amniotic fluid with cellular and sebaceous debris, meconium, or bacteria. The origin of abnormal amniotic fluid may be traced in numerous complications of labor, for instance, the occurrence of asphyxia and the escape of meconium into the fluid surrounding the fetus, premature rupture of the membranes, and prolonged labor. In this connection it is noteworthy that vaginal examination may introduce an additional hazard for the fetus as well as for the mother.

In evaluating the etiologic factors which are implicated in intra-uterine pneumonia it is obviously important to consider the extent to which the respiratory excursions of the fetal chest and diaphragm are effective in promoting a tidal flow of amniotic fluid between the amniotic sac and the interior of the lungs. If one resorts to experiment a clear-cut answer is obtained. For instance, in a rabbit in which the uterus was exposed by laparotomy, India ink was injected into the amniotic sacs of fetuses which were breathing as well as into the amniotic sacs of littermates in which respiratory movements had been abolished by injection of the fetuses with pentobarbital sodium. Examination of the lungs of the fetuses which had been breathing showed carbon particles in the pulmonary alveoli throughout the lungs even

within one minute after the addition of the ink to the amniotic fluid. In contrast, the lungs of apneic fetuses contained none.<sup>4</sup>

Furthermore, the findings in the lungs which have been reported in various series of autopsies<sup>13,14</sup> may readily be understood in the light of the active functioning of the respiratory organs before birth. Farber and Sweet<sup>15</sup> found amniotic sac contents in 88 per cent of the lungs of 124 infants surviving two hours to five weeks and presented evidence of a vernix membrane coating the pulmonary alveoli in some instances.

The significance of prompt expansion of the pulmonary alveoli immediately following birth is evident when comparison is made of the changes in the structure of the lungs obtained from fetuses which have not breathed air with those of infants which have breathed air.<sup>16</sup> Before birth the alveoli are partly dilated, being filled with amniotic fluid. After the breathing of air, there is a rapid increase in alveolar expansion. Adequate aeration is thus provided and the newborn is not drowned, since the elasticity of the alveolar walls permits an increase in the size of the alveoli of such magnitude that the surface area now obstructed by fluid becomes relatively greatly increased.

Atelectasis may arise during intra-uterine life by the breathing of abnormal amniotic fluid containing debris which obstructs and injures the respiratory passages. In case obstruction occurs at the time of delivery, there will be failure of alveolar expansion beyond the stage normally present within the uterus.

#### REFERENCES

1. POTTER and ADAIR. Factors associated with fetal and neonatal deaths. *J. A. M. A.*, 112: 1549, 1939.
2. BARCROFT. Respiratory and vascular changes in the mammal before and after birth. *Lancet*, 229: 647, 1935.
3. SNYDER and ROSENFELD. Direct observation of intrauterine respiratory movements of the fetus and the role of carbon dioxide and oxygen in their regulation. *Am. J. Physiol.*, 119: 153, 1937.
4. SNYDER and ROSENFELD. Intrauterine respiratory movements of the human fetus. *J. A. M. A.*, 108: 1946, 1937.



5. ROSENFELD and SNYDER. Factor of anesthesia in the pathogenesis of asphyxia neonatorum. *Am. J. Obst. & Gynec.*, 38: 424, 1939.
6. COLE, KIMBALL and DANIELS. Etiologic factors in neonatal asphyxia. *J. A. M. A.*, 113: 2038, 1939.
7. EASTMAN. Asphyxia neonatorum. *Internat. Clin.*, 2: 274, 1936.
8. CLIFFORD and IRVING. Analgesia, anesthesia and the newborn infant. *Surg., Gynec. & Obst.*, 65: 23, 1937.
9. SCHREIBER. Apnea of the newborn and associated cerebral injury. *J. A. M. A.*, 111: 1263, 1938.
10. MARCHETTI. Resuscitation of the newborn. *Am. J. Surg.*, 35: 259, 1937.
11. MURPHY. Negative pressure cabinet (respirator) treatment of asphyxia. *Am. J. Surg.*, 26: 354, 1934.
12. LIM and SNYDER. The response of the newborn to respiratory stimulants. *Am. J. Physiol.*, in press.
13. SLEMONS. Placental bacteremia. *J. A. M. A.*, 65: 1265, 1915.
14. WARWICK. Pneumonia in newborn and stillborn infants. *Am. J. M. Sc.*, 187: 253, 1934.
15. FARBER and SWEET. Amniotic sac contents in the lungs of infants. *Am. J. Dis. Child.*, 42: 1372, 1931.
16. SNYDER and ROSENFELD. Fetal respiration in relation to atelectasis and intrauterine pneumonia. *Am. J. Obst. & Gynec.*, 36: 363, 1938.



WHILE the total infant mortality has been reduced from 100 per thousand live births in 1915 to 54.4 per thousand in 1937, the neonatal (first month of life) death rate as well as the stillbirth rate has remained practically untouched.

From—"Fetal and Neonatal Death" by Edith L. Potter and Fred L. Adair (University of Chicago Press).

# OBSTETRICS AND GYNECOLOGY SYMPOSIUM

## GYNECOLOGY

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# GYNECIC PHYSIOLOGY AND THE GYNECOLOGIST\*

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IN no branch of medicine today does there exist a wider hiatus between experimental advance and clinical practice than that pertaining to the physiology of reproduction in the female—the fields of gynecic physiology, on one hand, and obstetrics and gynecology, on the other. The recent advances in this field of most general interest to the gynecologist are those which enable him to appreciate best the present status of the hormonal principles already available for use, and what systemic and local changes they elicit under particular conditions. The problem of the number, nature and interrelationships of the gonadotropic and sex hormones is basic for an understanding of the effects which such substances have, and so will be reviewed summarily.†

## THE GONADOTROPIC HORMONES

*Status.* The gonadotropic hormones are those which are capable of inducing directly characteristic changes, of a stimulating nature, in the gonads of suitable experi-

mental animals. Recent work has established that these may be classified, at the present time, into three groups.<sup>1,3,6,7</sup> The basis of the distinction between the several substances is largely biological, although chemical separation (by electrophoresis of suitable extracts, or by proteolytic digestion) may render the present simple grouping obsolete within a few years. Today, the gonadotropes are held to be: (a) of anterior pituitary origin; (b) chorionic origin; and (c) those typical of pregnant mare's serum, the active principles of which probably arise from the placenta.

None of the gonadotropes has been isolated in purified form, and all are standardized biologically by methods which are not exact in themselves nor uniform in various laboratories. Despite this fact, extracts are now commercially available, which, under highly restricted conditions, are said to be predominantly "follicle-stimulating" or "luteinizing." The utility of such extracts will necessarily depend upon their true effects on the human ovary and other tissues, and *these effects may not be accurately stated at the present time unless resort is made to specific enumeration without evaluation of endless experiments on subhuman and subprimate forms.* Van Dyke, discussing the gonadotropes in his recent book on the hypophysis, says: "Despite all the labor represented by a vast number of reports during the past few years, it is not yet possible to enumerate satisfactorily the gonadotropic hormones of the pituitary. Separate follicle-stimulating and luteinizing hormones are believed to exist."

One might point out that this belief is today complicated by two important conflicting facts. First, it has been shown

† Toward a solution of the problem of interpretation of this work, a number of recent books should be helpful, particularly to obstetricians and gynecologists. On the clinical side are books by Fluhmann,<sup>1</sup> Hamblen,<sup>2</sup> Sevringhaus,<sup>3</sup> Werner,<sup>4</sup> and Lane-Roberts et al.<sup>5</sup> These authors do not neglect the physiological aspect of the subject, but deal better and more fully with the clinical phases. These references will stand as beacons to those who desire detailed summaries of the present status of endocrine therapy in gynecology. In addition to these, other recent books deal with more basic aspects of reproductive phenomena in the female. Among these may be mentioned the second edition of *Sex and Internal Secretions*<sup>6</sup> written by a group of outstanding authorities; the recent second edition of the book by Van Dyke on the pituitary gland;<sup>7</sup> a third book on the physiology of the uterus<sup>8</sup> deals especially with the endocrine and other mechanisms of uterine motility, circulation, metabolism, innervation and growth. Hartman's book on the fertile period in women<sup>9</sup> and Dickinson's book<sup>10</sup> on the control of conception stand as the authoritative references dealing with these topics.

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that a corpus luteum, which undergoes degeneration as a result of hypophysectomy (through removal of a hypothetical luteinizing hormone), may be maintained by simple administration of an estrogenic hormone.<sup>11</sup> Second, hypophysectomy in a pregnant rabbit (which pregnancy normally terminates because of regression of the corpus luteum in such cases) may be compensated for by administration of estrogenic hormone,<sup>63</sup> as in the preceding instance. This effect is mediated through continuance of the corpus luteum by estrogen and not through the agency of a "luteinizing" hormone. There clearly exists, therefore, a gap which urgently requires bridging between data showing the existence of a specific luteinizing hormone, on one hand, and some which show such a substance to be nonessential, on the other.

The foregoing considerations may seem relatively unimportant and academic to the clinician, but they are fundamental to an understanding of the anterior pituitary gonadotropes. Consequently, "rational therapy" with such substances in ovarian hypofunction must await clarification of the nature and number of gonadotropic substance. *Hence, their use at this time is empirical and should be recognized as such in the evaluation of successes and of failures.* In spite of this, they are recommended by Hamblen<sup>2</sup> and Sevringhaus<sup>3</sup> for a variety of conditions (genital hypoplasia, hypoovarianism, delayed adolescence, menarche, sterility and meno-metrorrhagia). Parenthetically, one might observe that in the early development of most endocrine therapies, the successes find their way into the literature, the failures usually do not, and where success is claimed it is frequently not established that relief would not have occurred without intervention of endocrine therapy.

The gonadotrope, prolan, now coming to be called the chorionic gonadotropic hormone, is associated with human pregnancy, or neoplasms arising out of pregnancy. It is supposed to serve the purpose of sustaining the life of the corpus luteum,<sup>7</sup> although this

conclusion is prompted solely from the known action of prolan upon the gonads of mice, rats, rabbits and other laboratory animals. This gonadotrope has not been shown to be capable, when acting alone, of inducing luteinization in monkeys or women, and in those forms in which it does induce luteinization most readily, the placenta does not elaborate appreciable or even measurable amounts of such a hormone.

The relation of equine gonadotropes to prolan and anterior pituitary gonadotropes remains to be established,<sup>7</sup> along with some evidence of their clinical usefulness. Some reports have indicated recently that ovulation may be induced in women by adequate administration of equine gonotropes, although the published results to date are equivocal. Sufficient ovarian follicular stimulation has been produced in some women, however, to induce an "estrous-type" vaginal smear in selected women,<sup>12</sup> and pregnandiol excretion (see below) has been induced in cases of cyclic amenorrhea.

*Excretion of Gonadotropes.* Little may be said at this time regarding the ultimate value of gonadotropic substances in endocrine therapeutics, for the reasons mentioned above. There is no doubt that the most important aspect of current work lies in what is known of their presence in blood and urine under normal and abnormal circumstances, as a diagnostic aid. Their significance in the early determination of pregnancy (Aschheim-Zondek and Friedman tests), in the early establishment of ectopic pregnancy, and the detection of chorionepithelioma are cases in point. In such cases, the gonadotropes are present in sufficient quantity to permit the use of whole urine.

In the absence of pregnancy, the detection of gonadotropes in blood and urine requires special concentration (extraction) of the hormones. In normally menstruating women, data are conflicting, although it appears that a gonadotropic substance may be obtained in the mid-cycle, about the time ovulation is supposed to take place.

The importance of detecting anterior pituitary gonadotropes in the urine of women, however, lies not so much in the fact that it is detectable about the time of ovulation, but that it is far more abundant in urine obtained during afunctional conditions (e.g., operative castration, radiation castration, postmenopause, amenorrhea of long standing) as well as in certain hyperhormonal conditions (climacteric, irregular menses, polymenorrhea). According to Fluhmann,<sup>1</sup> it is seldom found (one case out of ninety-one) in hypohormonal cases (irregular menses, scanty menses, amenorrhea of short duration). The active gonadotropic substance in the urine of some menopause patients was at first thought to be follicle-stimulating only, although several later reports showed it to be "luteinizing" as well. For a detailed account of gonadotropes in various types of urine, the reader should consult the books by Fluhmann and Hamblen.

#### THE SEX HORMONES

*Terminology and Hormones.* There is probably no recent achievement in gynecic physiology of more direct value to the gynecologist than the clear establishment of the exact chemical nature and probable number of the sex, or gonadal, and related hormones. The number of native hormones is now known to be few, and these lend themselves to grouping into (a) gynecogenic substances, comprising both estrogens and progestogens, and (b) androgenic substances. The structural formulae of these and other important related substances are shown in Figure 1.

*Types of Response to Gynecogens and Androgens.* The actions which these substances have are so generally known that they scarcely require comment.

In a limited sense, an *estrogen* may be defined as a substance derived from natural, artificial or synthetic sources, which brings about in immature, ovariectomized or senile female animals growth of the accessory sexual glands, uterus, tubes,

vagina and breasts to normal (mature) or supernormal size. They are called estrogens since they are capable of simulating the specific histological and functional changes characteristic of estrus in certain laboratory animals.

A *progestogen* (Abarbanel<sup>13</sup>) is a substance which, acting upon a uterus first stimulated by an estrogen, causes further growth, marked glycogen deposition, secretion of the uterine glands, and hyperplasia of the glandular epithelium and of the muscular elements of the myometrium. All these changes are preliminary to, and necessary for, implantation and the maintenance of gestation, whence comes the name "progestin" devised by Corner and Allen. Progesterone also brings about relaxation of the pubic ligament, an effect heretofore attributed to a hypothetical hormone, "relaxin."<sup>14</sup>

An *androgen* is a substance which, when injected into an immature or castrated male animal, elicits extensive growth of the seminal vesicles, spermatic cord, prostate gland, penis, and Cowper's and the preputial glands. Such facts as these, however, are well known and fuller details are readily available to those who want them in modern textbooks of physiology, obstetrics and gynecology.<sup>65, 66, 67, 68</sup>

*Potency of Estrogens.* Other important facts concerning the relative potencies of various estrogens are not so well-known, however. Generally speaking, the several primary estrogens are, almost without exception, *qualitatively* identical in their effects, yet striking *quantitative* differences between them have been clearly established. Such differences are clinically important because they affect not only the time of onset (latent period) of a given response but also the amount of hormone (m. e. d.), and the duration of the response which a given mass of hormone will elicit. The latter is particularly important, clinically, since it governs the frequency with which the hormone must be administered. The following considerations show the difficulties which confront us since quanti-

tative differences in estrogenic potency were established.

When the relative effectiveness of a either of the other two substances. If,

### THE SEX HORMONES and SOME RELATED SUBSTANCES

	GYNECOGENS			ANDROGENS	
	Estrogens			Pregestogen	
PRIMARY SUBSTANCES	estradiol 	estrone 	estriol 	progesterone 	testosterone 
EXCRETION PRODUCTS (combined in liver with glucuronic acid, etc. relatively or completely inactive)	?	as an ester (a) in ovary (b) in uterus with progesterone	as an ester In absence of progesterone, increased destruction of these takes place in liver	pregnanediol allopregnanediol	androstosterone dehydroandrosterone
SOME RELATED SUBSTANCES chemically or biologically	cholesterol 	vitamin D <sub>3</sub> 	cholic acid 	equilin 	equilenin 
	methyl cholanthrene 	digitoxigenin 	corticosterone 		silibestrol 

FIG. 1.

number of estrogens was tested (uterine growth test), the following series was obtained<sup>15</sup> in decreasing order of effectiveness per unit mass of hormone: estradiol > estradiol benzoate > estrone > equilin > equilenin > estrone benzoate > estriol. Of these, estradiol, estradiol benzoate, estrone and estriol are commercially available, along with other estrogens. The order of this series is not basically important, however, because estriol, last in the series above, is the most potent estrogen when taken by mouth.<sup>2,6</sup> This is so because such a large proportion (up to 95 per cent) of other estrogens is inactivated when taken by mouth.<sup>16</sup>

Still another example of the difficulties encompassed by recognition of quantitative differences exhibited by various estrogens is shown by comparison, for example, of the relative strengths of estradiol, estradiol benzoate and estradiol dipropionate. Determination of the threshold dose (m. e. d.) of each of these substances

however, one considers the *duration* of the estrus induced by the same threshold mass of each hormone, the dipropionate ester is many times more effective than estradiol, while the benzoate ester is intermediate in this respect.<sup>17</sup> Many similar instances involving other estrogens and other tissue responses could be cited to corroborate the above points. All of them tend to show that, as our understanding of the chemical moieties of the sex-sterols has increased, standards for comparing their relative effectiveness have not been evolved.

The foregoing considerations show clearly the futility of attempting to gauge the relative potency of several estrogens on the basis of one phase of a twofold response—threshold and duration. On the other side of the problem, the question of route of administration, vehicle, and frequency of injections is equally important,<sup>49</sup> although in the work just cited, these factors were constant; only the hormone varied. In order to include the variables of threshold and dura-

tion of the response to estrogen in a single term or unit, Miescher, Scholz and Tschopp have suggested<sup>17</sup> the concept of the "work-output" and "activity coefficient" of an estrogen. This is based upon measurement of the area bounded by a standardization curve (uterine weight versus days) for a given preparation, and comparison of this planimetrically determined area with a similar area for any other preparation. The "coefficient of activity" is then expressible by calculating the ratio of one work-output to another work-output. Despite the obvious merit of such terms, this suggestion has not been generally adopted. Use of it would make it possible for the gynecologist to compare the estrogenic activity of one hormone with that of any other, a feat which is impossible by the present ambiguous standards.

This state of affairs requires one further word of explanation for those who confidently employ five or ten thousand international or rat units of an estrogen—any estrogen—in practice. The crux of the situation lies in the fact that two *different* international units have been formulated by the Committee on Hygiene of the League of Nations, one for estrone and one for estradiol benzoate. The "international unit" is 0.0001 mg. of each substance. In accordance with this, ampules of each will be labelled with the same number of *international units*, when the same amount, by mass, is in each. Nevertheless, by the Allen-Doisy rat test, or by the uterine growth test, estradiol benzoate is about one-half as potent as estrone in m. e. d., but it gives a much more prolonged response than the latter. Moreover, no international unit exists for most types of available estrogens (only estrone and estriol are listed in New and Non-official Remedies, 1939). Clearly, dosages of estrogens for clinical use based on such an artificial distinction are worthless to the physician.

The clinician may well ask what he is to do to obtain greatest effectiveness from a given dose, when the label on the box gives no true indication of the relative potency

of its contents. The answer is not easily given. The entire question of standardization should be reopened by the proper authorities, and a true basis for comparison agreed upon. In the meantime, the physician would do well to adopt some one type of estrogen in his practice, learn by experience how much and how frequently it must be given to obtain a desired effect. He would do well, perhaps, to be guided by the fact that esterification usually prolongs the action of an estrogen, while reducing its threshold for induction of estrus.

#### BISEXUAL POTENTIALITIES OF THE SEX HORMONES

As the atomic structure of the sex hormones and related sterols was established by a succession of brilliant studies in different laboratories and in various countries, our understanding of the nature of their effects in the mammalian organism became known. Broadly speaking the results showed bisexual effects of the hormones, although it was recognized that the several gynecogens and androgens exhibit a special predilection for specific reproductive tissues in females and males, respectively. The bisexual character of the hormones is suggested by studies of sex hormones in the urine of men and women and by the effects of injection of these hormones into both sexes.

*Gynecogens and Androgens in Urine.* In the urine of both men and women, gynecogens and androgens are found. A number of recent studies have been made on this and related topics, but those of Koch<sup>18</sup> may be cited as illustrative of the point as it is understood today. In men, there was found to be the equivalent of 4.0 mg. (40 international units of androsterone) per day excreted in the urine with an average daily excretion of estrogen amounting to 0.001 mg. (10 international units of estrone) in the same urines. Similarly, the urine of women showed appreciable quantities of both substances: of androgen, the equivalent of 2.6 mg. (26 international units of androsterone) was found, along with an



average daily excretion of estrogen equivalent to 0.0026 mg. (26 international units). Although two peaks of estrogen excretion occur during each normal (ovulatory?) menstrual cycle, no correlation was observed in the amount of androgen excreted at these same times (mid-interval and premenstrually). Androgen was found to be unusually high, however, in the urine of women with hypertrichosis.

The identity of the urinary androgens and estrogens has not been fully established. More will be said of these urinary estrogens below. Concerning the androgens, Koch says: "We know that androsterone and dehydroandrosterone are present in men's urine, but what relative amounts of these two substances are, is not known. Nothing definite is known as to the nature of the androgens in the urine of non-pregnant women." With regard to the estrogens, he says, "We are equally uncertain as to the chemical nature of the estrogens in men's and non-pregnant women's urines. The estrogenic material in men's urine however, shows the biological characteristics of theelin (estrone) and not of theelol (estriol)."

*Bisexual Actions of Injected Hormones.* The bisexual properties of a number of gonadal hormones have been investigated under a variety of conditions. The most extensive and systematic experiments are those of Korenchevsky<sup>19</sup> and his associates. The situation has been succinctly stated by him as follows: "These experiments on gonadectomized rats have established that nearly all the sexual hormones investigated tend to a greater or less degree to restore to normal both the male and female sexual organs, which have atrophied as a result of gonadectomy: a striking example is the most powerful of the male sex hormones, testosterone propionate. This brings about a return to normal, or even supernormal, of the atrophied sexual organs of castrated males. The same hormone also restores the structure of the atrophied uterus and vagina of an ovariectomized female to a condition not far from normal, while the

weight of the vagina and the development of some of the tissues of this organ is even supernormal. In normal rats, it stimulates the development of the uterus and vagina to much above the normal size and weight."

The relative effectiveness of the hormones, acting alone, in stimulating female sexual organs is as follows: estradiol > estrone > testosterone propionate > testosterone > androstanediol > androstenediol > androstendione > transhydroandrosterone > androsterone > progesterone. When the last named, progesterone, is administered with suitable amounts of estrogen, however, it compares with estrone and estradiol as a gynecogen. It is, moreover, to a certain degree androgenic, for under suitable circumstances it maintains or stimulates the prostate gland and seminal vesicles of castrated male rats. These accessory organs display secretory activity under such circumstances.<sup>64</sup>

Other, less direct, kinds of evidence have been adduced which demonstrate the bisexual potentialities of the gonads. An example of this is found in the observation that transplants of ovarian tissue into the ears of castrated male rats will sustain the accessory organs of reproduction, but not if the transplant is made into the warmer environment of the body. Vicarious gonadal function is not restricted to rats and lower animals. Thus, report was recently made<sup>20</sup> of a "perfectly formed and beautiful woman who possessed gonads which proved structurally and anatomically to be testes." The bearing of such conditions on varying grades of intersexuality is obvious, and they raise a question of whether hormone tests of blood and urine should be regarded as decisive diagnostic aids when corrective operations are contemplated. It is well-known that the surgeon's knife can oftentimes correct certain types of intersexuality. One can hardly refrain from making the observation in passing, however, that, quite aside from the correction of abnormal structure in sexual organs one ought also to consider the mental and social readjustment demanded of an individual

after the "corrective" operation is performed. In one classic case (masculinization from an adrenal tumor) studied by Young,<sup>21</sup> an individual who, in appearance, mental attitude, and sex-behavior was a male, possessed rudimentary female generative organs. When confronted by the decision that his sexual organs were potentially female, and that marriage with religious sanction to a woman was therefore out of the question, he chose self-destruction rather than undergo the mental and social reorientation which the necessary operation entailed.

From the standpoint of therapeutics with androgenic hormones, a number of recent reports suggest that testosterone or testosterone propionate may be useful in gynecological practice. The conditions in which it has been used successfully are: cyclic mastalgia, functional uterine bleeding, essential dysmenorrhea, premenstrual tension, the menopause syndrome, and relief of after-pains. In general, these reports are very favorable, and some are well-controlled. If, then, androgens are to become part of the armamentarium of gynecologists, one should question the wisdom of using a powerful agent which changes the voice, grows a beard, and may give rise to a masculine type of skeletal musculature and of mental outlook. The clinical reports now available frankly warn against such dangers. It is as yet too early to state what dosages may be employed safely in any given case and yet be therapeutically effective. It appears that masculinization may be detected<sup>22</sup> if dosages of some 500 to 600 mg. of testosterone propionate are used in a given course of treatment lasting some two weeks (as in the treatment of functional uterine bleeding); some reports<sup>13,23</sup> indicate that much smaller doses (40 to 60 mg.) may be effective in this condition without any undesirable side reaction. It may be pointed out that the principal factors which govern the level of androgen at which masculinization will be detected in any given case are not known. Consequently, androgen dosage must for

the present be empirical, and its effectiveness will depend upon the individual susceptibility of the patient to the hormone.

The problem of the ultimate utility of androgens in clinical practice therefore remains to be established. Any rational therapeutic efforts in this connection will take into account, however, the established effects which testosterone has upon the female organism. In the uterus of suitable rats, testosterone gives rise<sup>19</sup> to irregular structure of the stroma, vacuolation of the uterine epithelium, mucous cystic development of the endometrial glands, and an abnormal abundance of fibrous connective tissue in the myometrium. In the vagina, this hormone elicits deficient or irregular mucification, persistence of a narrow epithelium, and at best, only slight cornification with dropsical vacuolation and leucocytic invasion. In addition, testosterone causes growth of the clitoris, and marked development of perirethral glands into a "typical prostate." Still other important actions of androgens in the female have been established. For example, it will prolong gestation (i.e. inhibit parturition) in rats, and will prevent abortion after ovariectomy during pregnancy in lower animals, just as progesterone will do.<sup>8</sup> Also like the luteal hormone, it will inhibit menstruation in monkeys and women, and in rabbits, it will elicit progestational proliferation of the endometrium and will inhibit tubal and uterine motility. The most striking difference between testosterone and progesterone lies in the fact that the latter is much more efficient than the former; for certain of the above responses, a fivefold difference has been demonstrated. The systemic effects of androgens in the female resemble some of the systemic effects of estrogens. Thus they give relief from the vascular disturbances of the menopause and in many cases, they give rise to a general feeling of well-being.

At the present time it is impossible to visualize the rôle of androgens in the etiology of specific gynecological pathology, other than in cases of intersexuality, as

noted above. The fact that such substances are normal excretory products in the urine of women leads one to surmise, as Korenchevsky has done, that failure to consider the possible interplay of gynecogens and androgens is the basis of the failure, in the past, to interpret correctly the endocrine basis of a variety of common gynecological conditions. It is probable, therefore, that this new phase of gynecic physiology, which today complicates the problems of all who are engaged in this field of endeavor, will be tomorrow a stepping stone to the ultimate simplification of our understanding of the physiology of the sexual and reproductive cycle.

#### ARTIFICIAL ESTROGENS

*Stilbestrol.* A word must be said about a topic of increasing interest to, and discussion among gynecologists, namely, that of the status of artificial estrogens. Within the past few years, a number of substances have been obtained which bear no structural resemblance to the natural estrogens, i.e., no sterol nucleus (Fig. 1), yet they are highly estrogenic. Qualitatively, some of these substances compare with the natural estrogens in potency. The best known of these is stilbestrol. Some substances, it has been pointed out, are estrogenic only as regards certain limited aspects of the estrous response, and hence should be regarded as pseudo-estrogens. Stilbestrol, however, appears to be a true estrogen, according to the above definition, since it differs from natural estrogens in no important way in its biological effects on the female genital tract.

In view of the very low cost of production of stilbestrol in large quantity, and in view of its very high potency (especially when administered orally) and its similarity of action to natural estrogens, this substance lends itself readily to commercial exploitation. A considerable number of clinical reports are already in the German, English, and more recently, American literature.<sup>24,25,26</sup> The difficulty in appraising this literature lies in the highly contradic-

tory claims that have been advanced by various workers. There is no apparent basis for the divergence of views, and the Council on Pharmacy and Chemistry has been obliged to refrain from expressing an opinion on the acceptability of stilbestrol at this time.

All reports agree that stilbestrol is a very potent estrogen in women; that it is highly efficient when given by mouth, being but little inactivated in the processes of absorption and utilization (as natural estrogens are, especially in the human); that it is an effective agent in reducing the number and severity of menopausal flushes, and that it simulates natural estrogens in other important respects. There is *not* agreement, however, regarding the incidence of toxicity nor in the toxic manifestations which it elicits. The reserve which the American Medical Association maintains concerning stilbestrol is shown in the following partial quotation from a recent editorial.<sup>27</sup>

"The reports as to the toxic reactions of this substance are quite conflicting, some investigators stating that gastric distress is the only complaint, that this is experienced by from 5 to 10 per cent of the patients, and that it vanishes after a few days of administration. Others have found side reactions in greater numbers. One group of American investigators has observed as high as 80 per cent of the patients exhibiting untoward reactions, including cutaneous eruptions, psychosis, lassitude and liver damage. Apparently a thorough investigation of this compound is in order before it can be prescribed for routine therapy.

"The conflicts of reports on these substances and the opinions of some authorities on the possible harm from estrogen therapy should warn against long continued and indiscriminate therapeutic use of estrogens. Like numerous other therapeutic agents estrogens are effective under proper circumstances, but there may be definite danger when they are used unscientifically. In this connection the possi-

bility of carcinoma induced by estrogens cannot be ignored. The long continued administration of these proliferating agents to patients with a predisposition to cancer may be hazardous. The idea that estrogens are related in their activity only to the sex organs should be abandoned. Other tissues of the body may react in an undesirable manner when the doses are excessive and over too long a period. This point should be firmly established, since it appears likely that in the future the medical profession may be importuned to prescribe to patients large doses of high potency estrogens, such as stilbestrol, because of the ease of administration of these preparations."

#### SYSTEMIC EFFECTS OF ESTROGENS

The sex hormones are quite generally, though mistakenly, regarded as having effects which are confined to the secondary sex organs and to the development of secondary sex characters about the time of puberty. Such a view neglects the fact that these hormones may have other actions and that these, in turn, may have desirable therapeutic effects, or possibly undesirable ones; this will depend upon the nature of the effect and the condition of the individual. Such a view also fails to take account of the fact that the chemical configurations of the sex hormones bear a close relationship to a number of other physiologically and pharmacologically important substances. Examples of these are the life-sustaining adrenal cortical hormone, corticosterone, bile acids, ergosterol and the active vitamin D compounds, certain carcinogenic coal tar derivatives (e.g., methyl cholanthrene), and the active portions of some of the digitalis alkaloids. (Fig. 1.) It is safe to predict that the better-known systemic, or general, effects of estrogens, enumerated below, constitute but a small part of the total effects which these substances have throughout the body.\*

\* Among such other effects may be mentioned those of the relation of estrogens to certain allergies (Baker in *Canad. M. A. J.*, 40: 385, 1939); to polyarthritis

*Cardiovascular System.* The chief clinical use of estrogen for its general effects is in the treatment of the vascular disturbances of the menopause. While there is doubt about the specificity of its action in some cases, there is no question about the specific nature of the relief which it affords in the majority of cases. The basis for its effectiveness in the treatment of menopause conditions is not yet known. It has recently been established, however, that estrogens have a marked peripheral vascular action in some individuals and that this may be related to their therapeutic action. The evidence is both experimental and clinical, and may be reviewed summarily with profit.

While it is generally recognized that estrogens are without discernible effect upon the mean level of arterial blood pressure, or upon the heart, there is evidence that they have a vasodilating action on the smallest blood vessels in certain parts of the body.<sup>8,28,29</sup> The following facts suggest this: the injection of estrogen causes swelling and changes in the water content of the sex skin in certain primates; estrogen causes engorgement of the blood vessels in the nasal mucosa (see below); the injection of estrogen in the human is followed by a fall in capillary pressure and dilatation of the nail bed capillary vessels; estrogen causes a decrease of venous pressure in the hand; and, finally, estrogen causes a change in the water content of the skin of the rat within a few hours, qualitatively comparable to that occurring in the uterus and vagina.<sup>8</sup> More recent work shows that in a group of human males, estrogen likewise causes vasodilatation. The general features of the response are as follows: Within three to fifteen minutes, the volume of the finger begins to increase, sometimes after a transient vasoconstriction resulting from nervousness at the time of injection; the finger volume becomes steadily larger for at least half an hour,

(Radnor, in *Brit. M. J.*, 1: 505, 1939); and to susceptibility to infection (Sprunt and McDearman, in *Endocrinology*, 25: 308, 1939).

although more often the period of change lasts from forty-five minutes to an hour. The finger stays large for a period in excess of the maximum time of observation (two hours). The average percentage increase in finger volume was 4.6, although some 50 per cent of the finger is non-fleshy and so does not participate in the response.

The site of the vascular action of estrogen has been deduced from a number of related facts, all tending to show that the vasodilatation resulting from administration of estrogen involves the smallest blood vessels of the skin, namely, the capillaries and venules. For example, if arteriolar dilatation were involved, an increase in the rate of blood flow would occur and this should bring about an increase in the temperature of the skin, but such is not the case. Moreover, direct observation of the nail bed capillaries has shown that the smallest vessels are involved, although systolic and diastolic levels of blood pressure in the brachial artery are unaffected. This result could be accomplished in normal subjects only by vasodilatation beyond the arterioles. Finally, direct observation of the action of estrogen in the ear of the rabbit shows that vasodilatation involves the smallest vessels lying beyond the arterioles.<sup>29</sup> Since the condition of these vessels is not affected by denervation, the vasodilating action of estrogen in susceptible individuals must be mediated by some direct mechanism. It would appear to be significant in this respect that atropine inhibits the vascular effect of estrogen on the vessels in the rabbit's ear.

These vascular changes could hardly take place without some effect upon the heat regulating mechanisms of the body, since the chief function of the blood vessels in the human skin and in the ear of the rabbit is to assist in the regulation of heat loss by radiation.<sup>8</sup> Consequently, shifting blood into the skin (a shift must occur inasmuch as the peripheral dilatation occurs without a perceptible effect on blood pressure) should alter the capacity

of the body to lose heat with less need of sweating, especially under circumstances where nervous instability or increased heat production are concerned (e.g., emotion, excitement, effort). This is especially true of the rabbit where sensible sweating (i.e., perceptible water loss) does not take place and where the loss of heat from the body occurs largely in the ears. No appreciable change in skin temperature has been found in the human following administration of estrogen, signifying that the volume of blood in the skin increases without appreciable alteration in the rate of blood flow. In the rabbit, however, marked changes in the temperature of the ear occur, varying with the room temperature and the rectal temperature of the rabbit at the time of injection. Accordingly, the blood flow in the ear of the rabbit varies, not with the degree of vasodilatation, but with the requirements for heat loss which dilatation of the smallest vessels imposes on the normal temperature-regulating mechanisms under different experimental conditions.

The mechanism by which the vasodilating action of estrogen is exerted in the skin vessels of humans and rabbits has not been established. Some facts of an indirect nature support the idea that it may be associated with an increase in the tissues in the concentration of acetylcholine.\* Among these is the observation that the vasodilating action of estrogen in the ear of the rabbit can be inhibited by means of atropine, just as the hyperemia which estrogen induces in the uterus may be inhibited by means of this drug. Moreover,

\* Acetylcholine is a substance of great physiological importance. It appears to be liberated at motor and certain autonomic nerve endings by the arrival of nerve impulses. At these points, it is believed to constitute the excitatory agent between the nerve and effector organ, just as sympathin is known to do in certain parts of the thoracolumbar portion of the autonomic nervous system. Acetylcholine may be inhibitory, as in parasympathetic nerve effects on the heart and on certain blood vessels (i.e., vasodilatation), or it may be excitatory, as in vagus nerve effects in the gastrointestinal musculature. The work to which reference is made above is the first to show that certain hormonal effects may be mediated by acetylcholine (i.e., they are cholinergic effects).

it has been found that, within an hour after administration of estrogen to rabbits, the acetylcholine content of the uterus increases appreciably. This coincides with the onset of a pronounced vasodilatation in the uterus. Since this effect can be elicited in a uterus which is disconnected from the central nervous system (i.e., transplanted), and since the dilatation in the ear of the rabbit involves vessels whose activity is not affected by denervation, the dilating action of estrogens on the blood vessels of certain parts of the vascular tree is mediated by the setting up of local metabolic changes within the tissues in or around these vessels. Such changes involve, in one way or another, an increase in the amount of effective acetylcholine on the blood vessels.

The consequences of these vascular effects of estrogens upon the cutaneous circulation remain a matter of speculation. These vessels, it was noted above, are primarily concerned with heat loss from the body. Because of this, the view has been advanced that at least a partial explanation of the beneficial effects which estrogen exhibits in treatment of the vascular disturbances of the menopause is to be found in increased radiation of heat from the body.<sup>8,28</sup> This should minimize the need for intermediation of nervous factors, which result in sweating, and periods of temporary arteriolar dilatation, as occur in the menopausal flush. The basis of relief with estrogen is broader than this, however, since a large part of the improvement one sees lies in the regression of depressed mental states which are sometimes alarming.

*The Nasal Mucosa.* There is one other type of evidence that bears upon the peripheral vascular action of estrogen in the human, namely, the variations in color and thickness of the nasal mucosa under the influence of estrogen.<sup>8,30</sup> Periodic congestion of the nasal mucosa takes place in most women, varying in intensity in different subjects. Similar effects have been produced in monkeys treated with estrogens, and the response compares in inten-

sity of color with that which occurs during the normal menstrual cycle in this animal.<sup>31</sup> Recent work shows that the hyperemia of the nasal mucosa is probably associated with an increase in the effective amount of acetylcholine present. In the first place, acetylcholine is found in increased amount in nasal mucosa (in cats and rabbits) after injection of estrogen<sup>32</sup> and in the second place, patients with atrophic rhinitis may be successfully treated with estrogen, or, failing that, with prostigmine.<sup>20</sup> This drug specifically inactivates the enzyme cholinesterase, hence allowing acetylcholine to be free to exert demonstrable vasodilatation.\*

*Uterine Hyperemia.* Mention may be made in passing of the relation of the initial hyperemia which estrogen induces in the uterus to its other uterine effects.<sup>8,33</sup> Within twenty minutes to half an hour, dilatation of the uterine blood vessels is maximal, the vessels become increasingly permeable and water commences to accumulate in the tissues, especially in the endometrium. Afterwards, the oxygen consumption of the tissue increases, attaining a maximum level in about twenty-four hours. By this time too, the myometrium contracts intermittently, and mitotic proliferation of certain of the tissue elements begins. It thus appears that acetylcholine is a vasodilator substance acting upon the uterine tissues which are non-motile, which possess a low level of metabolism, and in which the blood vessels are of small caliber at the outset, so offering resistance to the rapid flow of blood through the tissue. By means of the initial vasodilatation in the uterus, a ready access of estrogen to the tissues is assured. Subsequently, other, anabolic effects of the

\* One should not conclude from the above discussion that estrogens will be found beneficial in the treatment of essential hypertension, Buerger's disease, Raynaud's disease, acrocyanosis and intermittent claudication. Some clinicians are coming to feel that estrogen may relieve incipient hypertension associated with the onset of the menopause, although it definitely is without effect on well-established or advanced hypertension. In the latter type of case, however, estrogen will relieve completely, or to a large degree, the flushes and involutional melancholia of menopausal origin.

hormone are effectively exerted upon the uterus.<sup>34</sup>

*Blood Constituents.* There is little published work on the true effects of sex hormones on the formed and unformed constituents of the blood. There exists, however, an abundance of data dealing with the blood picture during the menstrual cycle and pregnancy.<sup>1</sup> The situation is difficult to summarize, so conflicting are the various reports. These deal with an indicated decrease in the concentration of calcium, potassium, cholesterol, iodine and lecithin premenstrually. Other studies consider blood glucose, blood volume, hemoglobin, red blood corpuscle count and size, platelet count, and coagulation time. Concerning all these, Fluhmann aptly says, "The whole subject requires careful revision, and many published reports, presenting only a distorted view of the problem must eventually be discarded as useless. This criticism is particularly justifiable as applied to clinical studies because many authors have reached conclusions on totally incomplete and uncontrolled observations." The differences between males and females that are known to exist with respect to blood volume, red blood cell count and red blood cell size during puberty and later, suggest that investigations into the nature of these functional differences will prove fruitful.

*Oxygen Consumption.* In connection with the general oxygen metabolism, it is commonly recognized that sex differences exist. The greatest intra-individual differences occur in the female, the greatest inter-individual differences in the male. The reasons for the difference between males and females respectively have never been established.

With regard to levels of oxygen consumption during the menstrual cycle, recent work shows many contradictions.<sup>1</sup> This is exemplified by the following general claims regarding the rate of oxygen consumption during the menstrual cycle: (1) that it increases before and during menstruation;

(2) that it increases before menstruation; (3) that it decreases during menstruation and increases in the early interval; and (5) that it varies in no regular way.

If the relation of total oxygen consumption to the menstrual and sexual cycle is not clearly understood, it is, however, established that the sex hormones have marked and characteristic effects upon the metabolism in certain specific tissues. In animals, Victor and Andersen<sup>35,36</sup> and others<sup>37,8</sup> have made careful studies on the oxygen consumption and aerobic and anaerobic glycolysis of a number of isolated tissues of rats and mice in controlled sexual states. Among the tissues studied are those of the anterior hypophysis, liver, ovary, uterus, kidney, and a number of endocrine glands. The uterus exhibits periodic fluctuations in the levels of oxygen and glucose consumption. The significance of these changes cannot be stated at this time.

It is probably more interesting to clinicians that the uterus is but one of several organs exhibiting cyclic fluctuations in metabolism. Thus, the liver, ovary, anterior pituitary, and thyroid tissues all show periods of high oxygen consumption and of anaerobic glycolysis.<sup>36</sup> In pro-estrus, estrus, and during parturition (rats), the metabolism of these organs is higher than at other times. These cyclic fluctuations are abolished by spaying, and they may be simulated by injection of estrogen. The anterior pituitary gland responds first to the hormone, the thyroid second, and the liver third. When, therefore, Graafian follicles are rapidly maturing, the respiratory metabolism of a number of tissues in the body rises to a maximum. In view of the established histological relationships between the anterior pituitary gland and the ovary, on the one hand, and between the ovary and the uterus, on the other, it is probable that the heightened metabolic processes of the pituitary bear a causal relation to the concurrently elevated metabolism in the uterus. Because of the

rôle of the liver and a number of other tissues (thyroid, adrenal cortex, and isles of Langerhans) in carbohydrate metabolism, the periodic changes in carbohydrate metabolism in the liver may well contribute to the selective burning of carbohydrates in the uterus during estrus, as well as in other tissues.

The relationships, supposed and established, between sex hormones and fat metabolism lie beyond the scope of this article.

*Water and Salt Balance.* Not the least of the numerous effects of the sex hormones is their influence upon the water and salt content of various tissues. Just preceding the time of menstruation one may frequently observe a generalized edema, an increase in capillary fragility and a retention of sodium chloride.<sup>1,8</sup> Approximately one-third of normal women gain up to 3 or 5 pounds during the premenstruum. Soon after the onset of menstruation, there is return to normal weight. Careful studies on pregnant women have established that the water retention which occurs at this time is associated with retention of sodium chloride.<sup>38</sup> This is favored most particularly by estrogens, and involves tissues generally.

This fact is important, since current teachings in physiology hold that sodium in the body is almost entirely extracellular while potassium is largely intracellular. Moreover, when salt is retained by the tissues of the body there is marked water retention. Some individuals show a far greater dropsical tendency than others, for unknown reasons.

The effects which the gynecogens have on water and salt retention in tissues is shown by the strikingly opposite actions which estrogens and progestogens have in animals showing adrenal insufficiency. Progesterone, like corticosterone, will sustain life in, and restore moribund, adrenalectomized animals. Estrogens, on the contrary, are toxic under similar circumstances; they serve to hasten a crisis which only administration of large quantities of sodium

chloride or injection of cortical hormone or progesterone will relieve.<sup>39,40</sup>

No satisfactory explanation of these observations has as yet been made. They clearly point to the fact that the sex hormones, like the adrenal cortical hormone, contribute to those conditions now known to govern the water and electrolyte pattern of inter- and intracellular fluids. How this is achieved no one yet knows, although various theories suggest either that (1) the hormonal effect involves a primary regulating action on blood volume; (2) the permeability of endothelial tissues may be primarily affected by steroid hormones; (3) they have a "prepotent" action on carbohydrate metabolism; or (4) two or more of the above, along with other (endocrine?) factors may be involved.

The effect of estrogens in particular on the water content of tissues has been demonstrated in the case of the uterus (rat and monkey) and certain other tissues, especially skin and subcutaneous tissues.<sup>41,42,43</sup> When this hormone is injected into ovariectomized animals, the water content of the uterus increases measurably within six hours, after which a relatively greater increase in dry weight occurs. The first effect of estrogen, therefore, is to increase the amount of water in the intercellular phase of the uterus. This is nice confirmation of the histological interpretations of many workers, and it shows that, whatever its purpose may be, an increase in the amount of protoplasmic substance of the uterus is preceded by an appreciable hydration of the tissues.

Very careful measurements of the amount of water in the uterus of the monkey during selected periods of the menstrual cycle show that the changes in water content involve the tissues of the uterus as a whole, although the effects are most pronounced in the endometrium. In general, it may be said that, as the luteal phase advances, a reduction takes place in the water content of the mucosa of the corpus uteri, being most marked on the first day of menstua-



tion (see below). In the mucosa of the cervix, changes in water content are not pronounced. Although there are a number of conditions which contribute to the lack of a marked change in this region, it is pertinent to point out that menstruation involves only the endometrium of the corpus uteri, the cervix contributing nothing to the flow.

Along with the changes in water content of the uterus are other, equally marked, changes in the electrolyte pattern of the uterus. Present data show that in the follicular phase (rabbit), the concentrations of sodium and calcium are at a maximum, the potassium and magnesium at a minimum. In contrast, during the luteal phase, conditions are reversed. The functional significance of these changes is a matter of speculation.<sup>8</sup> For the present, it is sufficient to note that the several sex hormones produce effects upon the retention and partitioning of water and specific ions in the make-up of uterine tissues.

All in all, therefore, these hormones, and the estrogens in particular, may be said to possess characteristic actions upon both uterine and certain systemic tissues. As in the case of the peripheral vascular action of estrogens, it appears that those effects which are well known and pronounced in the reproductive tissues are reflected in miniature throughout other parts of the body. To what extent considerations such as these should be considered in the treatment of obstetrical and gynecological problems (e.g., toxemias of pregnancy) only time will tell.

*Skin Pigmentation.* At the present time, only the following fact is known for a certainty concerning the relation of sex hormones to pigmentation in the skin: If hypogonadal individuals (male or female) are exposed to sunlight, they fail to tan readily although an invisible change takes place in the tissue. Thus, if androgens or estrogens are injected subsequent to exposure to ultraviolet light (up to several months) pigmentation of the skin occurs without further exposure to light. Injection

of the hormones into non-photosensitized individuals fails to elicit pigmentation.<sup>44</sup>

The relation of this phenomenon to the mechanism of carotene and melanin deposition is unknown. It is perhaps suggestive that the sex hormones have a sterol nucleus somewhat similar to that of adrenal cortical hormone, in the absence of which coloration of the skin characteristic of Addison's disease takes place.

The reported beneficial value of estrogens in some types of acne may ultimately find its basis in connection with some of the underlying skin metabolism and vascular changes mentioned above.

*Oxidation-Reduction and Sex Hormones.* Reference is made to this topic to call attention to a phase of uterine physiology which, because of its relation to the very life of tissues, is important in health, and so in disease. There is little one may say at this time, however, regarding the presence of specific enzyme systems of the uterus and other tissues on which the sex hormones act in order to regulate the necessary energy for various aspects of uterine functions. In the case of the uterus, energy is required for such diverse phenomena as growth (including hypertrophy and hyperplasia), repair of tissue, secretion, activation and inhibition of myometrial motility and finally, sensitization of the mucosa for the decidual reaction.

Two enzyme constituents of the uterus, ascorbic acid (vitamin c) and glutathione, have been specifically investigated.<sup>8</sup> Ascorbic acid is present in the uterus when active mitotic proliferation is under way. The concentration of glutathione bears an inverse relation to ascorbic acid: it is present in lowest concentration in the proliferative stages, and highest at other times (rabbit). Studies by Pincus and his associates have established that glutathione is necessary for the phase or phases in early pregnancy of tubal and uterine function in which the life of the ovum is sustained by secretory activity of the lining epithelium of the genital tract; for this, progesterone is necessary.

At present, these and related observations that might be cited stand as isolated facts, the significance of which can only be surmised in a general way. One of the greatest advances in physiological chemistry in recent years deals with chemical reactions which, by the breakdown of products of intermediary metabolism, release energy to the tissues. At each step in the oxidation of these various substances, energy becomes available through an electronic change; the action is aided by specific hydrogen carriers, aided in turn by enzyme systems to combine ultimately with oxygen. This substance is activated by specific enzyme systems (cytochrome and yellow oxidase). For each step, and for each substrate, special enzymes must be present to act, for without them the metabolic processes cease to be normal or to progress to completion. Considerations such as these suggest that it is in the determination of the kind and distribution of enzymes, or in the local conditions under which these systems work, that the sex hormones govern the several aspects of reproductive function.

Despite the fact that so much of uterine physiology, biochemistry and histology is known, little attention has as yet been paid to this fundamental aspect of gynecic physiology. Until it is, the mechanisms by which the several hormones exert their respective effects will remain obscure. It seems safe to say that the greatest advances in the future in gynecic physiology lie along these lines. With this thought in mind, we therefore turn to the prevalent ideas regarding the nature of the intermediary metabolism and excretion of estrogens and progestogen respectively.

*Metabolism of Gynecogens. Interconversion of Estrogens.* There are three primary estrogens, estrone, estradiol, and estriol. Of these, estradiol is most potent on injection, and is believed, therefore, by many to be the true follicular hormone. The interrelationship between these native hormones is now so well established that it is perhaps superficial to regard any one as the

"true" hormone, when all play a part in the manifestations of estrus. Recent work by Pincus and his associates, which is briefly summarized below, indicates the extent to which this is so.<sup>45,46</sup> The following general facts may now be stated with assurance:

1. Estriol is an end product of estrone and estradiol conversion in the body (rabbit). This is exemplified in part by the fact that when estriol is injected into rabbits in virtually any sexual state (in heat, pregnant, pseudopregnant, hysterectomized in heat, hysterectomized-pseudopregnant, or recently ovariectomized) the urinary estrogen is recoverable as estriol only. It is not modified by ovarian activity or the state of the uterus. The amount of estrogen recoverable in proportion to the amount injected, however, is definitely affected by ovarian activity; thus the percentage recovery is much increased by the presence of progesterone.

2. Estrone is modified when injected into rabbits according to the condition of the reproductive tract. Thus, in rabbits that are in heat, pregnant, or pseudopregnant, both estrone and estriol are recoverable in the urine. After ovariectomy of long standing, or after hysterectomy (with the ovaries present or absent), however, only estrone is excreted upon injection of estrone. It therefore follows that estrone is converted into estriol in the uterus, and for this to take place, the uterus must be under active ovarian control, since several months after castration, conversion does not take place. Regardless of whether estrone or estriol is excreted in the urine, the total estrogen recoverable represents only a fraction of that which is injected; consequently, destruction of estrone as well as of estriol takes place *in vivo*.

3. Regarding destruction of estrogens in the body, it seems certain that the liver is primarily involved. This is suggested by the fact that benzylation (i.e., esterification) allows almost complete recovery of the hormone in the urine. Moreover, when ovarian transplants which have not been

effective on the mesentery are relocated at a site where the portal circulation is circumvented, they become highly effective.<sup>47</sup>

4. Estradiol is found in only minute amounts in the urine after injection of estrone into rabbits; there is, therefore, little conversion of the ketone into the diol form. After the injection of estradiol, however, estrone is the preponderant hormone excreted, although estriol may be present if the ovaries are in the luteal phase, or if progesterone is injected. This conversion of estradiol to estrone occurs only if functional ovarian tissue is present, and is unaffected by the presence or absence of uterine tissue. The conclusion therefore follows that estradiol, the "true" follicular hormone, is rapidly converted into estrone; this substance is, in turn, partially inactivated by the liver, partially excreted as such, and partially converted into estriol, provided that functional uterine tissue and progesterone are present.

5. Progesterone has important effects upon the metabolism of estrogens, as mentioned above. It increases the quantity of estrogen excreted in the urine, presumably through a sparing action of the estrogens from destruction by the liver enzymes. How this is brought about is not known. Pincus suggests that perhaps progesterone is more readily attacked by the same liver enzymes that inactivate estrogens, so increasing the quantity of the latter hormones available for urinary excretion. It is considered certain that the effect of progesterone is mediated through a sparing action, and not through a change in kidney threshold to estrogens. Progesterone's second action is in the conversion of estrone to estriol, where it acts in conjunction with functional uterine tissue.

The foregoing facts offer a nice explanation for the well known increase in blood and urinary levels of estrogen in the latter (luteal) part of the menstrual cycle. This phenomenon has been heretofore difficult to explain on the basis of an active follicular phase in the first part of the cycle, associated with a low level of estrogen

excretion. It now appears that in the early interval there is a different type of estrogen metabolism involving a high degree of estrogen destruction. Estrogen production continues at a high level throughout the menstrual cycle, with increased excretion, as progesterone spares it from destruction by the liver.<sup>48</sup>

Two other aspects of progesterone metabolism in the endometrium deserve mention: it gives rise to glandular growth and permits ovum growth. Together, these include, among other things, mitotic hyperplasia, glycogen deposition, secretion and sensitization of the endometrium for nidation. The effect of the several primary estrogens on each of these endometrial effects of progesterone is not identical.<sup>49</sup> For example, the presence of an excess of estrone, combined with simultaneous administration of progesterone, inhibits both gland growth and ovum growth but it affects the latter response first. Estradiol and estriol, in contrast, inhibit glandular growth without affecting ovum growth directly. "It is a matter of some moment," Pincus and Werthessen write, "that estrone inhibits both egg growth and glandular proliferation, whereas [estradiol and estriol] do not . . . while definitely decreasing the degree of glandular proliferation. It indicates that [estradiol and estriol] are not involved in exactly the same reactions as estrone."

*Mechanism of Estrogen Action.* A number of considerations of the foregoing sort suggest that in the uterine metabolism of estrogens, a chain, or group, of reaction systems acts upon, or requires the participation of, the hormone molecules. It is supposed<sup>49</sup> that because of this chain of related reactions, many points are available for synthetic substances of suitable configuration to act, and so exert an estrogenic effect from that point in the chain. This theory offers a basis upon which the fact that numerous substances of varying molecular configuration (such as stilbestrol, tetrahydrophenanthrene, etc., etc.) can exert pseudoestrogenic effects of varying

degrees. This is exemplified in the following statement by Pincus and Werthessen: "The vaginal effect presumably occurs at a point in the chain wherein rather wide variation in chemical structure does not necessarily hinder activity. Participation in certain of the uterine reactions on the other hand requires more specific structural configuration; the reactions involving ovum growth, for example, are unaffected by certain native hormones which do affect both uterine proliferation and vaginal activity."

*End Products of Progesterone Metabolism.* The end products of the metabolism of progesterone in the body are just beginning to be worked out. The situation does not lend itself to brief summary.<sup>2</sup> It is likely that pregnandiol (combined in the liver with glucuronic acid) is the principal urinary end product of such metabolism in the human.<sup>50,51</sup> In general, this substance is present in the urine during the latter part of the menstrual cycle. It is recoverable (about 40 per cent of the theoretical amount) after injection of progesterone in ovariectomized women and normal males.<sup>52</sup> It has also been found in the urine of a male with Addison's disease.<sup>52</sup> Finally, it is present in human urine throughout pregnancy, even after ovariectomy early in pregnancy. This signifies that progesterone is produced in human pregnancy outside the corpora lutea, most probably in the placenta (Venning and Browne).

There is doubt concerning the site at which progesterone is converted into pregnandiol. Some investigators find that after injection of a small amount of progesterone into hysterectomized women (with the ovaries present), no pregnandiol is recoverable in the urine; others find that larger amounts of progesterone given to similar women yield pregnandiol. This has been regarded as indicative of the rôle of the liver in conversion of progesterone to pregnandiol.

There are a number of difficulties encountered in regarding pregnandiol as the sole end-product of progesterone metabo-

lism, even in women. First, some women may excrete pregnandiol in the absence of a well-marked premenstrual endometrium; second, some women with premenstrual endometria may not excrete pregnandiol; and third, pregnandiol is not found in the urine of laboratory animals (rabbit, monkey), even after the injection of progesterone. Since less than half of injected progesterone is recovered in the urine of women, a large share of it remains to be accounted for. The present methods of extraction measure only pregnandiol-glucuronidate and not free pregnandiol or other combined forms, nor do they measure any other end-products which may be present. There are, it is estimated, more than ten probable end products of progesterone metabolism in the body.

*Carcinogenesis and Estrogens.* One reads with increasing frequency of carcinogenesis as a danger to be recognized in prolonged estrogen therapy. The essential facts in this regard will therefore bear enumeration.

In the first place, it is possible to produce carcinomata in mice—but only mice thus far—by injecting estrogen for long periods of time in immature female or mature male mice of strains in which most of the females develop mammary cancer between the ages of six to twelve months.<sup>53</sup> The tumors lead to death within about six weeks after the first appearance of small, palpable nodules. Such tumors induced by estrogens in males are truly carcinomatous, since bits of this tissue transplanted to untreated males grow into tumors which are lethal without further estrogen treatment. In immature females subject to prolonged estrogen treatment, cervical cancer may be produced if the mammary cancer, which invariably appears first, is repeatedly trimmed away. According to Edgar Allen (personal communication), the total quantity of carcinomatous mammary tissue thus removed may appreciably exceed the total weight of the animal itself. Fibromyomata have been produced experimentally in guinea pigs by prolonged (up to

eight months) estrogen therapy, but not in mice, rats, rabbits or monkeys.

To summarize, true carcinomata have only been produced in strains of mice which have a strong genetic susceptibility to carcinoma; without this genetic factor, estrogens have never been shown to be carcinogenic.<sup>53</sup> To date, only mice have proved susceptible to this aspect of estrogen action. Finally, one should note that other factors operate which may predispose toward or against growth of carcinoma resulting from estrogens in susceptible strains of mice. Thus, an essential oil (heptyl aldehyde) added to food decreases the incidence of certain types of malignant tumors in mice.

#### UTERINE PHYSIOLOGY: SOME RECENT ADVANCES

*Uterine Growth Stimuli.* Two types of normal growth stimuli are recognized for the uterus: hormones (chemical) and distention (physical).<sup>8</sup> Of the former, estrogens elicit marked hyperplasia of connective tissue elements in the uterus, with subsequent conversion into smooth muscle elements (neogenesis). They have no known effect on mitotic division in smooth muscle fibers, although they bring about extensive hypertrophy of all constituents of the uterus. Estrogen favors extensive mitosis in the epithelium of the endometrium in normal growth and repair.

Progesterone has somewhat different effects, in addition to the well known progestational proliferation of the endometrial glands. It is the hormone par excellence for causing mitotic division of the smooth muscle elements of the myometrium; it does not, however, favor hypertrophy of these tissues. The bearing of the differing predilections of estrogens and of progesterone on connective tissue and smooth muscle in the uterus, respectively, on specific gynecological conditions is not clear. They are facts, however, which may prove useful in future gynecologic studies dealing with the etiology of abnormal uterine growths.

In addition to hormonal stimulation of uterine growth is the second one of uterine distention. The latter has been demonstrated by insertion of pellets of suitable size into uteri of untreated, ovariectomized rabbits.<sup>8</sup> Within four days after such a procedure, marked and characteristic uterine growth effects take place. These include increase in the amount of fluid throughout the entire region of distention, and mitotic hyperplasia and hypertrophy of the myometrium in particular. The effect is not traumatic, for it is devoid of any evidence of leucocytic infiltration.

When distention is combined with estrogens and progesterone, an unexpected change in the growth response takes place. With estrogen, the distention-growth response is absent, and with progesterone, it is diminished by about 50 per cent. The nature of the mechanisms involved in each of these responses<sup>8</sup> and their relation to uterine growth during pregnancy need not be reviewed here. It suffices to point out that, so far as the gynecologist is concerned, the effects of uterine distention (induced by insertion of stem pessaries) on the size of the hypoplastic uterus and on ovarian hypofunction is old knowledge (Dickinson and Smith).

*Uterine Cervical Changes.* Cyclic fluctuations in uterine cervical secretions have been recognized for some time. Their relation to the transport of spermatozoa through the cervix has only recently been demonstrated.<sup>54,55</sup> Lamarr and his associates have estimated in women during the menstrual cycle the quantity, viscosity, pH, leucocytes, and sperm-penetrability of cervical mucus. They found that the extent to which spermatozoa penetrate this fluid varied with several measurable factors, and that it is limited to a few days in the middle of the cycle. It is at this time that ovulation is believed to occur in women.

During these few days, cervical mucus is most abundant, the pH is highest (up to 7.5), few leucocytes are present, and the viscosity is lowest. In view of current teachings that uterine contractions are not

necessary for, and probably are not a factor in, sperm entry into the uterus,<sup>8</sup> the control (by hormones) of optimal conditions in cervical mucus may be deemed important in the treatment of sterility in women when other sterility factors are absent.

*Vaginal Smears.* Much is being written in certain journals concerning the usefulness of vaginal smears as a diagnostic aid in the evaluation of hypo-ovarian function, or of the effectiveness of follicular hormone therapy.

Characteristic smear-types may be obtained from the human vagina, not unlike those obtainable from certain laboratory rodents. Papanicolaou, who, with Stockard, discovered vaginal cycles in guinea pigs in 1917, reported<sup>56</sup> this phenomenon in women in 1933. With Shorr, he demonstrated<sup>16</sup> in 1936 its applicability in evaluating the effectiveness of estrogen therapy.

The technique is not difficult to carry out, but it must be meticulously followed for satisfactory results. According to Shorr (personal communication), the failures other clinicians have encountered are attributable to uncritical attempts at simplifying the procedure of obtaining or staining the smears. Saline is admitted to and retrieved from the vagina by a pipette inserted 5 to 6 cm. beyond the vaginal orifice. The fluid is put on a slide, dried, placed in an alcohol-ether mixture, and then successively taken through alcohol dilutions into distilled water. Staining is carried out in successive stages, through Ehrlich's hemotoxylin, eosin, and water-blue. The smear is evaluated by judging the amount of mucus, the number of leucocytes, the number of erythrocytes, clearness of the smear, the number of deep and superficial cells, the grouping characteristics of the cells and the number of cornified cells in the smear. For important details of this technique, one should consult the original articles<sup>56,16</sup> since this procedure lends itself readily to office practice with only minor laboratory facilities.

*Menstruation Mechanisms.* The causes of menstruation are unknown. While it was

thought a few years ago that a special "bleeding hormone" of the anterior pituitary was involved, this view is now discredited. The immediate stimulus for menstruation in all probability resides within the uterus. This is shown by the fact that menstruation begins at different times in various parts of the endometrium. Two important questions therefore arise, namely, what local tissue changes precede the onset of menstruation, and by what mechanisms do the several gynecogenic hormones control these changes? The succession of brilliant studies by Markee<sup>57,58</sup> give the answer to the first question, while theories of various investigators<sup>59,8</sup> must suffice, for the present, to answer the second.

A necessary condition for menstruation in monkeys is a period of intense ischemia of the superficial portion of the endometrium. This lasts for some twelve hours and is associated with, or followed by, prominent and characteristic changes in the endometrium. Thus, there is marked thinning of the endometrium, loss of water and increased coiling of the spiral arteries with hemostasis. These changes are followed by leucocytic infiltration of the superficial stroma and subsequent necrosis. The typical papilla, hemorrhage and repair follow.

Among the foregoing local tissue changes, there are two which *must* occur if menstruation is to take place; the blanching is indirect cause of them both. One is that thinning of the endometrium must take place, the other, that spiral arteries be present to give rise to increased coiling of, and hemostasis in, the blood vessels of the superficial stroma.\*

The phenomenon of thinning of the endometrium begins late in the blanching (ischemic) period and exhibits important variations. It may take place so slowly that little, if any, bleeding occurs. If thinning is

\* The spiral arteries have been described in detail by Daron<sup>60</sup> and by Bartelmez.<sup>59</sup> These structures arise from the vascular zone in the myometrium, pass through the basal zone which is separately supplied by non-spiral vessels.

precipitous and extensive, however, the duration and rate of blood flow will be great. Abnormal manifestations of the former would thus occur as amenorrhea or oligomenorrhea, of the latter as menorrhagia. If the change occurred aperiodically, it would be classed as metrorrhagia.

It is important to note that the *rate* of endometrial thinning is governed by the rate at which the influence of the gynecogenic hormones is withdrawn, while the *extent* of the thinning is determined largely by the thickness which the endometrium has attained during the interval, at the time of uterine growth. We may turn in conclusion, therefore, to the nature of the hormonal conditions which are associated with the onset of menstruation, for on a proper understanding of this will rational therapy of menstrual disorders largely depend.

*Menstruation and Hormonal Factors.* As mentioned above, the flow of menstrual blood is governed in part by the extent to which the uterus has grown in the interval between menstrual bleedings. This is determined to a great extent by the proper association of hormonal and dietary factors, the first of which have been considered briefly in the first part of this article. What is said below refers more particularly to hormonal factors immediately associated with the onset of menstruation.

Menstruation may be induced in monkeys and in women by a variety of methods.<sup>6,8,59</sup> Thus, it occurs soon after withdrawal of the hormone in a course of estrogen treatment in ovariectomized monkeys or women; it occurs after ovariectomy during a functional cycle (except when the operation is performed on the first day of menstruation); it takes place when the level of estrogen is lowered during a course of injections; and finally, it occurs after the withdrawal of progesterone during a course of injections. The onset of menstruation may be inhibited by other procedures. Thus, progesterone (or testosterone), given immediately following any of the foregoing procedures but the last, inhibits the estab-

lishment of menstrual bleeding until the progesterone is withdrawn. Estrogen will delay the menstruation associated with ovariectomy, but not that which follows withdrawal of progesterone. It should be noted once again that the common physiological denominator for all these various conditions is the state of the superficial portion of the endometrium, as mentioned in the preceding section.

There is one important modification in the method of inducing menstruation which Zuckerman<sup>61</sup> and Corner<sup>62</sup> have separately described. They noted that in addition to local conditions within the uterus which are responsible for the blanching, there are also periodic systemic changes of an as yet undefined nature which affect the sensitivity of the uterus to hormonal stimulation. The observation is this: if ovariectomized monkeys are given small, constant amounts of estrogen daily, week in and week out, uterine bleeding occurs periodically. This can only mean, that at such times a change within the system occurs which renders the endometrium unsusceptible (i.e., raises the uterine threshold) to the constant level of estrogen. This would then be functionally comparable to the experimental withdrawal of the gynecogenic hormones, which the earlier experiments in monkeys and in women have merely simulated. Consequently, it appears unlikely that a "cause" for menstruation will ever be discovered; rather, it is more probable that a number of related and interdependent local and systemic conditions will be found indispensable in this phenomenon.

#### REFERENCES

1. FLUHMAN, F. L. *Menstrual Disorders: Pathology, Diagnosis and Treatment*. Philadelphia, 1939. Saunders.
2. HAMBLIN, E. C. *Endocrine Gynecology*. Springfield, 1939. Thomas.
3. SEVRINGHAUS, E. L. *Endocrine Therapy*. Chicago, 1939. Year Book Publishing Co.
4. WERNER, A. A. *Endocrinology, Clinical Application and Treatment*. Philadelphia, 1937. Lea & Febiger.

5. LANE-ROBERTS, C., SHERMAN, A., WALKER, K., and WIESNER, B. P. Sterility and Impaired Fertility. New York, 1939. Hoeber.
6. ALLEN, E., DANFORTH, C. H., and DOISY, E. A., editors. Sex and Internal Secretions, 2nd ed. Baltimore, 1939. Williams & Wilkins.
7. VAN DYKE, H. B. Physiology and Pharmacology of the Pituitary Body, 2nd ed. Chicago, 1939. University of Chicago Press.
8. REYNOLDS, S. R. M. Physiology of the Uterus, with Clinical Correlations. New York, 1939. Hoeber.
9. HARTMAN, C. G. The Time of Ovulation in Women. Baltimore, 1936. Williams & Wilkins.
10. DICKINSON, R. L. Control of Conception, 2nd ed. Baltimore, 1939. Williams & Wilkins.
11. WESTMAN, A., and JACOBSON, D. Über oestrinwirkungen auf die Corpus luteum-Funktion. *Acta obst. gynec. scandinav.*, 17: 476, 1937.
12. SHORR, E., and PAPANICOLAOU, G. N. Action of gonadotropic hormones in amenorrhea as evaluated by vaginal smears. *Proc. Soc. Exper. Biol. & Med.*, 41: 629, 1939.
13. ABARBANEL, A. R. Treatment of functional uterine bleeding with testosterone propionate. *Am. J. Obst. & Gynec.*, in press.
14. HATERIUS, H. O., and FUGO, N. W. Relaxation of the pelvic ligaments of the guinea pig induced by progesterone. *Proc. Soc. Exper. Biol. & Med.*, 42: 155, 1939.
15. DORFMAN, R. I. The comparative activity of various estrogens on the infantile rat uterus and vagina. *J. Biol. Chem.*, 31: xxiv, 1937.
16. SHORR, E., and PAPANICOLAOU, G. N. Action of ovarian follicular hormone in the menopause, as indicated by vaginal smears. *Am. J. Obst. & Gynec.*, 31: 806, 1936.
17. MIESCHER, K., SCHOLZ, C., and TSCHOPP, E. Activation of female sex hormones. *Biochem. J.*, 32: 141, 725, 1273, 1938.
18. KOCH, F. C. Recent advances in the field of androgens. *Cold Spring Harbor Symposia on Quant. Biol.*, 5: 34, 1937.
19. KORENCHESKY, V. Bisexual properties and cooperative activity of sexual hormones and their effects on females. *Brit. M. J.*, 2: 917, 1937.
20. Editorial. Sex hormone therapy. *Brit. M. J.*, 2: 917, 1937.
21. YOUNG, H. H. Genital Abnormalities, Hermaphroditism and Related Adrenal Diseases. Baltimore, 1937. Williams & Wilkins.
22. GEIST, S. H., SALMON, U. J., and GAINES, J. Use of testosterone propionate in functional uterine bleeding. *Endocrinology*, 23: 784, 1938.
23. RUBINSTEIN, H. S. Rationale of use of testosterone propionate in functional uterine bleeding and dysmenorrhea. *J. Lab. & Clin. Med.*, 24: 1026, 1939.
24. SHORR, E., ROBINSON, F. F., and PAPANICOLAOU, G. N. A clinical study of stilbestrol. *J. A. M. A.*, 113: 2312, 1939.
25. BUXTON, C. L., and ENGLE, E. T. Effects of diethyl stilbestrol therapy. *J. A. M. A.*, 113: 2318, 1939.
26. MACBRYDE, C. M., FREEDMAN, H., and LOEFFEL, E. Studies on stilbestrol. *J. A. M. A.*, 113: 2320, 1939.
27. Editorial. Estrogen therapy, a warning. *J. A. M. A.*, 113: 2323, 1939.
28. REYNOLDS, S. R. M., and FOSTER, F. I. Peripheral vascular action of estrogen in the human male. *J. Clin. Investigation*, 18: 649, 1939.
29. REYNOLDS, S. R. M., and FOSTER, F. I. Peripheral vascular action of estrogen, observed in the ear of the rabbit. *J. Pharmacol. & Exper. Therap.*, 68: 173, 1940.
30. SOSKIN, S., and BERNHEIM, L. B. Mechanism of estrogen effect on nasal mucosa in atrophic rhinitis: successful treatment with prostigmine. *Proc. Soc. Exper. Biol. & Med.*, 42: 22, 1939.
31. MORTIMER, H., WRIGHT, P., BACHMAN, C., and COLLIP, J. B. Effect of administration of oestrogenic hormones on nasal mucosa of monkey (*macaca mulatta*). *Proc. Soc. Exper. Biol. & Med.*, 34: 535, 1936.
32. REYNOLDS, S. R. M., and FOSTER, F. I. Unpublished observations.
33. REYNOLDS, S. R. M. Nature of uterine contractility; a survey of recent trends. *Physiol. Rev.*, 17: 304, 1937.
34. REYNOLDS, S. R. M. Acetylcholine-content of uteri before and after administration of oestrin to ovariectomized rabbits. *J. Physiol.*, 95: 258, 1939.
35. VICTOR, J., and ANDERSEN, D. H. Effects of oestrus and spaying on the metabolism of the pituitary. *Am. J. Physiol.*, 115: 130, 1936.
36. VICTOR, J., and ANDERSEN, D. H. Comparison of tissue metabolism in normal, spayed, spayed-thyroidectomized and hypophysectomized female rats. *Am. J. Physiol.*, 122: 296, 1938.
37. KERLY, M. Effect of oestrous cycle on metabolism of isolated rat uterus. *Biochem. J.*, 31: 1544, 1937.
38. TAYLOR, H. C., WARNER, R. C., and WELSH, C. Relationship of estrogens and other placental hormones to sodium and potassium balance at the end of pregnancy and in the puerperium. *Am. J. Obst. & Gynec.*, 38: 748, 1939.
39. GAUNT, R., and HAYS, H. W. Life-maintaining effect of crystalline progesterone in adrenal-ectomized ferrets. *Science*, 88: 576, 1938.
40. GAUNT, R., NELSON, W. O., and LOOMIS, E. Cortical hormone-like action of progesterone and non-effect of sex hormones on "water-intoxication." *Proc. Soc. Exper. Biol. & Med.*, 39: 319, 1938.
41. ASTWOOD, E. B. A six-hour test for the quantitative determination of estrogen. *Endocrinology*, 23: 25, 1938.
42. KROHN, P. L., and ZUCKERMAN, S. Water metabolism in relation to the menstrual cycle. *J. Physiol.*, 88: 369, 1937.
43. VAN DYKE, H. B. Biochemical changes in reproductive organs in relation to their physiology. *Ergebn. Physiol.*, 38: 836, 1936.
44. HAMILTON, J. B. Significance of sex hormones in tanning of skin in women. *Proc. Soc. Exper. Biol. & Med.*, 40: 502, 1939.
45. PINCUS, G. Metabolism of ovarian hormones, especially in relation to the size of the fertilized ovum. *Cold Spring Harbor Symposia on Quant. Biol.*, 5: 44, 1937.
46. PINCUS, G., and ZAHL, P. A. The biogenesis of primary sex hormones. I. The fate of estrins injected into the rabbit. *J. Gen. Physiol.*, 20: 879, 1937.



47. GOLDEN, J. B., and SEVRINGHAUS, E. L. Inactivation of estrogenic hormone of ovary by liver. *Proc. Soc. Exper. Biol. & Med.*, 39: 361, 1938.
48. SMITH, G. S., and SMITH, O. W. Observations concerning metabolism of estrogens in women. *Am. J. Obst. & Gynec.*, 36: 769, 1938.
49. PINCUS, G., and WERTHESSEN, N. T. An analysis of mechanism of oestrogenic activity. *Proc. Roy. Soc. London, B*, 126: 330, 1938.
50. VENNING, E. H. Gravimetric method for determination of sodium pregnandiol glucuronidaet (excretion product of progesterone). *J. Biol. Chem.*, 119: 473, 1937.
51. VENNING, E. H., and BROWNE, J. S. L. Study of metabolism of progesterone. *Am. J. Physiol.*, 123: 209, 1938.
52. BUXTON, C. L., and WESTPHAL, U. Recovery of pregnandiol in urine of men treated with progesterone. *Proc. Soc. Exper. Biol. & Med.*, 41: 284, 1939.
53. ALLEN, E. Some recent studies of reproduction and associated endocrines. *Yale J. Biol. & Med.*, 12: 51, 1939.
54. LAMARR, J. K., et al. *Am. J. Physiol.*, in press.
55. SJOVALL, A. Untersuchungen über die Schleimhaut der Cervix Uteri. *Acta obst. & gynec. scandinav.*, 18: suppl. 4, 1, 1938.
56. PAPANICOLAOU, G. N. Sexual cycle in human female as revealed by vaginal smears. *Am. J. Anat.*, suppl., 52: 519, 1933.
57. MARKEE, J. E. Menstruation in ocular endometrial transplants. *Anat. Rec.*, suppl. 55: 66, 1933.
58. MARKEE, J. E. Relation of uterine regression to menstrual bleeding in intra-ocular transplants in rhesus monkey. *Anat. Rec.*, suppl., 70: 54, 1938.
59. BARTELMEZ, G. W. Menstruation. *Physiol. Rev.*, 17: 28, 1937.
60. DARON, G. H. Arterial pattern of the tunica mucosa of the uterus of the macacus rhesus. *Am. J. Anat.*, 58: 349, 1936.
61. ZUCKERMAN, S. Menstrual cycle of primates. xi. Part played by oestrogenic hormone in menstrual cycle. *Proc. Roy. Soc. London, B*, 123: 451, 1937.
62. CORNER, G. W. Quantitative studies of experimental menstruation-like bleeding due to estrin-deprivation. *Am. J. Physiol.*, 124: 1, 1938.
63. ROBSON, J. M. Maintenance of pregnancy in hypophysectomized rabbits by administration of oestrin. *J. Physiol.*, 95: 83, 1939.
64. GREENE, R. R., BURRILL, M. W., and IVY, A. C. Progesterone is androgenic. *Proc. Soc. Exper. Biol. & Med.*, 40: 83, 1939.
65. BEST, C. H., and TAYLOR, N. B. *Physiological Basis of Medical Practice*, 2nd ed. Baltimore, 1939. William Wood.
66. WIGGERS, C. J. *Physiology in Health and Disease*, 2nd ed. Philadelphia, 1939. Lea & Febiger.
67. WRIGHT, S. *Applied Physiology*, 6th ed. New York, 1936. Oxford University Press.
68. BECK, A. C. *Practical Obstetrics*, 2nd ed. Baltimore, 1939. Williams & Wilkins.



# ENDOCRINOPATHIC AMENORRHEA: CAUSES AND TREATMENT\*

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**A**MENORRHEA refers to the absence of recurring periods of menstrual bleeding at approximately one month intervals. Amenorrhea before the menarche, during pregnancy, and after the menopause is controlled by endocrine forces. When amenorrhea occurs under other conditions it is frequently due to morbid endocrine situations. These include several subtypes, such as (1) delayed menarche; (2) hypoplasia of genitalia; (3) ovarian hypofunction, with or without obesity; (4) postpartum amenorrhea and sterility; (5) premature climacteric. Unfortunately the differentiations between these diagnostic groupings are not as precise as the words suggest. Experience with a large number of women complaining of amenorrhea will be certain to include some instances which might as reasonably be placed in any one of these five categories as in the group mentioned before or after it. In other words, this series of diagnostic terms represents, rather than qualitative differences, merely quantitative variations in the activity of anterior pituitary and ovarian secretions. The exact diagnostic differentiations often involve use of facilities and training which are not at present available to the general practitioner. It may, nevertheless, be of interest to present for general medical readers the diagnostic and therapeutic methods currently in use for the handling of patients with amenorrhea. Most such cases when detected by the general practitioner should be seen in consultation by the gynecologist especially experienced in endocrine work, and should

be treated over a period of months by the two in collaboration.

Histories need to be taken in careful detail as to menstrual rhythm and fertility.<sup>1</sup> Physical examinations may reveal many contributory facts about the endocrine status of the woman. But the skillful bimanual pelvic examination is indispensable. If it leaves any uncertainty it should be repeated under simple general anesthesia. At this stage in examination plans should be laid for securing endometrium, either with the curette or one of several types of biopsy instrument. From the microscopic study of this tissue, correlated with the interval since the onset of the last menstrual flow, much can be determined about the nature and intensity of the ovarian hormone secretion. Thus far the methods are available to any physician practicing gynecology. Limitations on the diagnostic study of the endometrium are being obviated by recent reports of the types found under such circumstances,<sup>2</sup> so that competent pathologists can now learn to discriminate types of endocrine action.

In those clinics where special attention is given to this field of endocrine disturbances in gynecology there are several laboratory methods being used increasingly to advantage. One is the study of the stained smear of vaginal mucosal cells.<sup>3</sup> This is not extraordinarily difficult, but interpretation requires some experience not easily put into print, although easily acquired by observation with someone who has this experience. Another method is the assay of urine specimens for pituitary and ovarian hor-

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mones. The assay methods suffer from lack of sensitivity, paucity of data obtained from normal women, and great cost. Assays must be restricted for some time yet to research clinics.

Accessory technical methods frequently of use are x-ray study of the sella turcica region, examination of visual fields for evidence of neoplastic lesions adjacent to the optic chiasm, and basal metabolism measurements. Amenorrhea rarely is associated with a pituitary tumor, but the possibility must be kept in mind until eliminated by the x-ray and eye examinations. The Cushing syndrome is striking and not easily overlooked. Basal metabolism determinations are probably misused more frequently than omitted. Unless there is good clinical evidence of hypothyroidism associated with lowered metabolic rate in cases of amenorrhea, it is wise to seek confirmation by the determination of blood cholesterol. Although the x-ray and basal metabolic rate are available in every hospital, blood cholesterol is not so widely in use. Where dependable blood chemical work can be done this is worth adding to the repertoire of the laboratory.

#### DELAYED MENARCHE; PRIMARY AMENORRHEA

In the northern parts of the United States the menarche occurs between 12 and 15 years of age. The average is 14, and, of course, healthy girls occasionally begin menstruating before 12 or after 15. Therefore, it is considered unwise to initiate therapy for delayed menarche until after 15. Exceptions may well occur if there is no sign of adolescence during the 12 to 15 year period, indicating that maturity is much delayed. If the delay in onset of menstruation becomes significant, a careful pelvic examination should be made to determine whether the genitalia and especially the uterus and ovaries are present. Although this seems rudimentary, it is still being omitted. If such examination leaves a question in the mind of the examiner that there may be rudimentary ovaries and a

uterus which cannot be felt, a therapeutic test is now possible. The procedure used in this clinic is most easily illustrated by a case.

A girl of nearly 17, who was referred because of primary amenorrhea, had very small breasts but was otherwise a well built, healthy young woman. History and physical examination gave no clues to a cause for amenorrhea. School history, basal metabolism, and blood cholesterol determination agreed in eliminating hypothyroidism. She had been seen by three physicians, none of whom had made a pelvic examination. Under anesthesia no ovaries were palpable, a cervix was seen, but no uterus could be felt, and even with a curette no tissue was obtainable from the very shallow cavity entered through the cervix. Since there was doubt about the existence of ovaries a therapeutic test was undertaken. Daily injection of 100 units of pituitary gonadotropic extract (prephysin) was continued for fifteen days, and repeated after an interval of two weeks. Vaginal epithelial smears obtained before and after this therapy showed no evidence of estrogenic effect. The cells were of the type characteristic of the deeper layers of vaginal mucosa. The conclusion drawn was that if ovaries were present in this girl, they were rudimentary, and the prognosis for establishing the menses was considered extremely dubious. No further therapy was advised. It is obvious that such a prognosis could not be expressed with any confidence unless there had been previous experience with the same gonadotropic extract to justify confidence in its potency. The next case will illustrate this.

A woman of 25 was admitted to the psychiatric service because of numerous personality problems, including her fear that she was "turning into a man." The family and referring physician believed permanent institutional care necessary. The history of primary amenorrhea led to a suggestion of endocrine study. The patient refused to allow a pelvic examination, even by a woman. Vaginal smears were obtained, and were typical of castrate mucosa. Thereupon she was given 100 unit doses of prephysin daily for fifteen days. After two days estrogenic activity was in evidence, and a marked change had appeared after ten days. Four days following the interruption of this therapy her first menstrual flow began and con-

tinued for seven days. These events indicated that she had ovarian and uterine tissues, and that the gonadotropic extract was potent. Another course of therapy caused a second flow three weeks later. During the following eight months she received six further series of treatments. No flow occurred, although she made striking psychologic improvement, and was able to leave the hospital after the first flow. The vaginal smears continued to show moderate estrogenic activity, and a curettage obtained ten months after the first therapy showed low intensity of glandular growth, with some areas of cystic glandular hyperplasia. The uterus was obviously small. Two brief menstrual flows occurred within the following month, but during the next twenty-six months, in spite of persistent use of cycles of treatment, no further flows have been observed. On four occasions treatments have been interrupted and each time there has been gradual relapse of the psychic status, followed by a good recovery when therapy was resumed. Vaginal smears have continued to indicate estrogenic response to the use of prephysin, and similarly to the gonadotropic (maturity) extract of Armour or of Ayerst, McKenna and Harrison, and to pregnant mare serum concentrate, gonadin, of the Cutter Laboratory. It will probably never be possible to stimulate the ovaries in this woman to the point of fertility, but sustained treatment has served to rehabilitate her psychologically and economically, which is justification for its continuance.

The prognosis in primary amenorrhea is poor if pituitary secretion is so low that one must supply all the gonadotropic stimulation hypodermically, and if the gonads are infantile. Perhaps better forms of gonadotropic therapy will become available.

#### HYPOPLASIA OF GENITALIA

The cases of primary amenorrhea cited above have had poorly developed internal and external genitalia. Similar hypoplasia may be associated with secondary amenorrhea, with infrequent, scanty, irregular menses, or with menorrhagia. These are probably various manifestations of the same underlying hypofunction of pituitary and ovaries as previously described.<sup>4</sup> One

special case is that of the woman whose amenorrhea is complicated by asthenia, loss of weight, hypotension, and numerous nervous complaints. It is in such patients that one finds difficulty in deciding between anorexia nervosa and Simmonds' cachexia. The onset is usually insidious. There are seldom anatomic findings which indicate pituitary involvement. Occasionally the psychologic problem is obvious, more often it requires patient search to find why the woman will not or cannot eat an adequate diet to maintain normal weight. Detailed study of several such patients has failed to reveal evidence for hypothyroidism or adrenal deficiency, or for chronic infection.

Endometrium is usually scanty, with few glands, and no evidences of progestational changes. Vaginal mucous membrane is not of the castrate type, but shows less cornified cells than expected for the age of the woman. The menstrual flow has often been absent for many months or several years. Use of potent gonadotropic extracts in large doses repeated for several consecutive months has been surprisingly futile in this type of patient. Intensity of estrogenic response has not increased, judged by vaginal smears, endometrial biopsies, occurrence of flows, or subjective changes. It appears that these women are not without ovarian activity, but that for some reason their ovaries fail to respond.

In a few cases we have been able to demonstrate in the urine of such women as much gonadotropic hormone as is found by the same technique in young women with regular menstrual cycles. We, therefore, incline to group these patients as anorexia nervosa, and to attribute the amenorrhea and hypoplasia to prolonged undernutrition. That this is not an entirely satisfactory explanation is suggested by the fact that severe undernutrition of large portions of the population because of economic stringency has not usually produced amenorrhea. Probably there is a combination of undernutrition and some other inherent individual factor leading to the genital hypoplasia and asthenic state. To date no

success has attended endocrine therapy in this condition.

#### HYPOFUNCTION OF OVARIES

Secondary amenorrhea may occur with grossly normal genitalia, including a well developed uterus. If this hypofunction is associated with obesity, it constitutes one type of the Fröhlich syndrome. The obesity is by no means essential, and when overweight is a problem it must be treated by dietary restriction and increased exercise as in any other patient. The prognosis in such cases is often good if gonadotropic therapy is used.

A woman of 19 was referred because of amenorrhea for six months, and sterility since marriage at 16. Menses had begun at age 12; the duration of flow had gradually declined from three days to complete absence of bleeding, but leucorrhea was present. Moderate obesity had developed slowly. There were few symptoms resembling the climacteric. Basal metabolic rate was plus 18. Pelvic examination was in no way remarkable. Endometrium was easily obtained with a biopsy punch, but showed very little activity, no mitotic figures, and a dense stroma. The patient began use of prephysin in 100 unit doses daily for fifteen days, and was sent home. Menstruation did not occur. She had been told to repeat the series of injections beginning with onset of the next flow, or after a month if no flow appeared. After three months her referring physician reported her probably pregnant, and her delivery occurred nine months after the only series of gonadotropic injections. Lactation was satisfactory.

The restored fertility in this patient seemed surprising, but similarly prompt response to therapy has occurred in several women. It cannot be expected as the rule. More frequently repetition of the treatments at monthly intervals appears necessary. If regularity of rhythm shows improvement, if vaginal smears show increasing evidence of estrogen action, if symptomatic improvement is definite, gonadotropic therapy may well be repeated at monthly intervals for several years. Since

the cyclic activity of the ovaries increases beginning at about the time of onset of a menstrual flow, we choose this date as the most appropriate one for resuming the successive series of hypodermic injections. We have consistently avoided using continuous daily treatment, to prevent developing cystic ovaries. Instead we have employed from five to fifteen doses, distributed over five to fifteen days of the cycle. If flows do not recur at intervals of at least six weeks, we feel justified in resuming therapy without longer intervals.

Amenorrhea and other evidences of hypofunction of pituitary and ovaries may depend on secondarily depressed action due to hypothyroidism or adrenal insufficiency. Examples will illustrate the way in which pituitary gonadotropic therapy may help even such cases.

A student, aged 20, was examined because of change from her usual four week cycles to the occurrence of only two menstrual flows in thirteen months. She was at least 35 per cent overweight, had a basal metabolism of minus 14, and pelvic examination showed a small and retroverted uterus. Endometrium, obtained ten weeks after the last flow, resembled that found after castration. It was felt that the diagnosis was more probably the Fröhlich syndrome than hypothyroidism. Use of gonadotropic injections, 25 units of prephysin, led to resumption of menses. The number of doses was increased to five daily doses followed by five on alternate days, beginning at the onset of each flow. Improvement was evident from the first, and after eighteen months cycles were substantially regular of the four weeks type. Following twenty-six months' therapy the gonadotropic injections were stopped, and cycles have continued very dependably regular. Weight control was not facilitated, and, therefore, after six months without treatment the use of thyroid was begun and has been continued with better weight control, as well as with slightly shorter and more uniform duration of flow.

In considering the responses of such a patient it is impossible to determine whether the primary fault was hypothyroidism or hypopituitarism. It has been

noted in animal experiments that if thyroid function is depressed, the anterior pituitary shows cytologic alterations<sup>5</sup> which might easily be responsible for such alteration of function as this patient showed. The Fröhlich syndrome is not usually accompanied by evidences of hypothyroidism, but it is possible that at times the decreased function of the pituitary may affect the gonads and also the thyroid. In practice it is probably wise to use thyroid therapy as the first approach only if and when there is good clinical evidence of thyroid deficiency. If success is not achieved gonadotropic therapy may be added. Similar reasoning applies to the less frequent adrenal insufficiency, or mild Addison's disease. The effects of long continued adrenal insufficiency are illustrated by the following case:

A woman, aged 34, had considered herself well until the previous four years, during which interval she had several attacks marked by vertigo, nausea, and hypotension. Complaints included fatigue from slight exertion, weakness, tremors, backaches, scotomata, paresthesias, palpitation, and constipation. Menstruation began at 14, had been of a regular four week type, but with gradual decrease in duration of flow from age 20 until amenorrhea occurred at age 31 after the symptoms became markedly severe. A miscarriage occurred at age 21, after which no further conception had been possible. When first seen at age 34, she was in a remission of the Addison's disease, which was still demonstrable by studies of blood volume and serum sodium response to salt restriction. Menses were recurring but at intervals of three to five weeks. Endometrial biopsy showed a progesterational reaction, which was characterized as degenerative in appearance. Following a period of some two years use of added salt and potent adrenal cortex extract, menses were restored to a regular four week rhythm of four to five days flow. Fertility has not been restored. This woman is believed to have had a long-standing adrenal deficiency, probably of the atrophic rather than the tuberculous type. The depressing effect on ovarian function is parallel to the general asthenic picture, and both have shown good response to adrenal therapy, without use of either estrogen or gonadotropic hormone.

#### POSTPARTUM AMENORRHEA AND STERILITY

The reports of Sheehan<sup>6</sup> have called attention to the probable mechanism involved in the irregularities of menstruation, amenorrhea, and loss of fertility which not infrequently follow pregnancy. As with other lesions, there are quantitative variations in the extent of the disturbance produced. Examples will illustrate the varied prognosis depending on the extent of the depression in endocrine function.

A woman of 33 years had one child born two years before, after which her menses were no longer of the regular monthly type, but occurred at approximately three month intervals, associated as never before with prolonged dysmenorrhea. Fertility was reduced. Obesity, acne, abdominal pains, as well as hot flashes, sweating attacks, dyspnea, headaches, weeping, worrying, paresthesias, and self-depreciation had appeared after the puerperium. Physical findings were not remarkable aside from moderate obesity, which was controlled by diet, and blood pressure 138/110. Pelvic examination discovered bilateral moderate enlargement of the ovaries, and retroversion of the uterus, which was corrected by a pessary. The endometrium obtained on the twenty-eighth day of a fifty-two day cycle was not typical of any stage in the normal cycle. Estrogenic activity was apparent but of varying and low intensity, with some mitotic figures seen. It was felt that the differential diagnosis lay between premature menopause and postpartum hypopituitarism. Due to the early age and the desire for further children, an effort was made to stimulate the ovaries by the use of pregnant mare's serum concentrate (gonadogen), given ten units hypodermically on alternate days. After a total of twelve such doses, in three cycles, with three menstrual flows occurring at intervals of four and seven weeks, the patient became pregnant and went to term. She was given progesterone as a measure of safety during the first trimester. Subsequent to the second pregnancy menses were again irregular and infrequent. Menorrhagia led to hysterectomy, at which time cystic ovaries were found and removed, but the symptoms suggestive of the climacteric have no longer been evident.

The favorable outcome of this case is to be contrasted with the persistent difficulty in a 24 year old woman after birth of a child at age 19. Delivery was followed by a syndrome resembling surgical shock. Menses were always irregular after that, and ultimately led to amenorrhea at age 23. Other symptoms were occasional hot flashes, marked asthenia, weeping, morbid worrying, insomnia, and self-depreciation. The breasts were almost constantly painful, and some swelling was noted. Blood pressure was 90/60, basal metabolism minus 13 per cent. Under anesthesia the uterus was found to be distinctly small, and endometrium was obtained with difficulty with the curette, the tissue appearing typical of the castrate. Vaginal epithelium obtained by the smear technique showed very slight estrogenic activity. The patient was started on a program of pituitary gonadotropic injections, using 100 units of prephysin daily for ten doses. Vaginal smears showed a slight, but distinct response, which was not progressive. After three such courses of treatment in three months the vaginal response was not improved and no flow appeared. There was no significant symptomatic change. It was, therefore, concluded that the extent of pituitary failure was so profound that the amount of therapy necessary to reestablish menses and fertility would be impractically large. It was advised that treatment should be limited to sufficient amounts of estrogen to relieve symptoms.

#### PREMATURE MENOPAUSE

There is difficulty in distinguishing between the last case and the occasional spontaneous cessation of menses earlier than the middle of the fifth decade. It is assumed that the menopause refers to cessation of ovarian secretion of hormones because of inability of the ovaries to respond to gonadotropic stimulation.<sup>7</sup> The gonadotropic secretion of the pituitary is probably increased at and after the climacteric, judged by microscopic appearance of the anterior lobe,<sup>8</sup> by gonadotropic hormone content of the human gland in older women, and by the sustained high gonadotropic hormone excretion in the urine of women during and after the menopause.<sup>9</sup> When the failure of menses is due to pitui-

tary failure as in the two cases cited above, we incline to exclude them from the premature menopause group. By contrast we would place the next patient in this latter diagnostic classification. We hope that assays of urine gonadotropic hormone output will assist in this separation. Preliminary findings indicate that when this hormone output is higher than during the usual fertile period of the third and fourth decades it is probable the ovaries cannot longer respond to gonadotropic stimulation. Such a conclusion will require more extensive validation before it will be dependable.

A woman, aged 35, was referred because of sterility. She was in excellent health and symptom-free, but her usually regular menses had been interrupted for five months. Vaginal smears were examined at intervals of a few days for three months. There were slight fluctuations in estrogenic activity, and menstrual flows occurred at intervals varying from three to six weeks. The use of gonadogen was begun, first with six doses of 10 units each during the first two weeks after each flow began, later with 20 units per dose and as much as 300 units per cycle of therapy. There were occasionally spurts of encouraging increase in estrogenic response shown in the vaginal smears. During one such cycle chemical determination of pregnandiol in twenty-four-hour urine specimens<sup>10</sup> showed the output of 45 mg. in seven days, indicating that ovulation had occurred. Nevertheless, there were only four flows in the succeeding year, and none in the year following. Attempts to induce ovulation during periods of amenorrhea by combining hypodermic administration of gonadogen with intravenous injection of 50 to 60 units after two weeks of such stimulation were futile. No pregnandiol was excreted. Flow did not follow within two weeks. Therefore, treatment was discontinued because it was felt that the ovaries in this woman had become so refractory to stimulation that their period of activity was essentially over. Increased supply of gonadotropic hormone by injection produced too little response to justify continued therapy. This situation constitutes a premature menopause.

In the patient just described there were no climacteric symptoms, in spite of the

very low estrogenic hormone production by the ovaries. The same statement applies to many women at the usual climacteric age. On the other hand, we have seen women as young as 20 in whom premature climacteric symptoms have appeared in violently disturbing intensity, associated with postpartum amenorrhea. It is apparent from these observations and from more recent urinary assays<sup>9</sup> that the occurrence of climacteric symptoms is independent of the pituitary gonadotropic hormone production in menopause states.

#### THE MENOPAUSE

After the menopause, fertility is not desired, and it is obvious that there is no value to be gained by stimulating the ovaries. If unpleasant symptoms are present, the amenorrhea is to be ignored, and the patient treated symptomatically. Usually this requires the administration of an estrogenic substance. If estrin is given in sufficient doses, and with brief periods of interruption, menstrual flows can be re-established. Such flows are of interest in arriving at an understanding of the mechanism of menstruation, but from the patient's point of view the production of a flow is merely a nuisance. It can be avoided by the use of minimal doses of estrogen administered at regular short intervals, rather than large doses given less frequently. The necessary duration of such therapy may be from a few weeks to a few years. Since it can be done simply, safely and economically by oral administration of estrogens, this is at once the commonest and simplest of all types of treatment for "amenorrhea." Of course, the reason for treatment is not the amenorrhea, but the symptoms.

It is possible to treat these same symptoms similarly when associated with menstrual irregularities during the earlier decades. There is far less prospect of re-establishing menstrual regularity and fertility than if gonadotropic therapy is employed. For this reason we continue to urge that estrogenic hormone be used

chiefly for relief of climacteric symptoms, when there is no intent to restore fertile and regular menstrual rhythm.

#### ENDOCRINE MATERIALS

Our earliest and most extensive experience has been with prephysin, the commercial product, by the Chappel Laboratory, of the extract from the horse pituitary, originally described by our former colleagues, Hisaw and Fevold.<sup>11</sup> This is available in two concentrations, containing 25 or 100 units per c.c., distributed now by the Harvey Company. The disadvantage of prephysin is that it usually causes local inflammatory reactions, due to the protein materials present. A more limited use of the maturity or gonadotropic extract of the Armour or Ayerst, McKenna and Harrison Laboratories has convinced us of its dependable activity. The inflammatory reactions are not so marked as with prephysin, but this advantage is counterbalanced by the lower potency of the material. The unit employed for this material is very much smaller than for prephysin. We have been gratified by the results from pregnant mare's serum concentrate. This has been used in two forms: gonadogen from the Upjohn Laboratory is dispensed in dry tablets, in sterile vials, with saline for solution at the time of injection; gonadin from the Cutter Laboratory is in aqueous solution, and must therefore be refrigerated when not used promptly. These materials cause little or no local inflammatory reaction. In our experience there has been no important allergic reaction to gonadogen or gonadin, and very little to prephysin. We prefer to avoid the use of the concentrates of human pregnancy urine in the treatment of amenorrhea, for this gonadotropic material does not stimulate follicular activity.

For generous supplies of the five gonadotropic extracts described we are indebted to the manufacturers who have thereby made possible the study of an extensive series of patients.



## SUMMARY

Amenorrhea may result from failure of the ovaries to respond to pituitary gonadotropic stimulation, or from deficient pituitary secretion. Ovarian failure is characteristic of the menopause, and is to be treated for symptomatic control only, and by the use of estrogenic substances. Pituitary inadequacy may be substituted for by gonadotropic substances obtained from animal pituitary or from serum of pregnant mares. Hypodermic injections of these extracts are advised in series of five to fifteen doses, during the first two weeks of the menstrual cycle, or at intervals beginning not oftener than every four weeks, to attempt reestablishment of cyclic flowing. Determination of the ability of the ovaries to respond is facilitated by the use of vaginal smears showing the estrogenic effects on vaginal mucosa.

## REFERENCES

1. ENGLE, E. T., and SHELESNYACK, M. C. First menstruation and subsequent menstrual cycles of pubertal girls. *Human Biol.*, 6: 431, 1934.
2. CAMPBELL, R. E., LENDRUM, F. C., and SEVRINGHAUS, E. L. Endometrial histology and pathology as revealed by the biopsy method. *Surg., Gynec. & Obst.*, 63: 724, 1936.
3. PAPANICOLAOU, G. N., and SHORR, E. Action of ovarian follicular hormone in the menopause, as indicated by vaginal smears. *Am. J. Obst. & Gynec.*, 31: 806, 1936.
4. SEVRINGHAUS, E. L. Treatment of gonadal hypofunction. *Bull. N. Y. Acad. Med.*, Feb. 1940.
5. SEVRINGHAUS, A. E., SMELSER, G. K., and CLARK, H. M. Anterior pituitary changes in adult male rats following thyroxin injections or thyroid feeding. *Proc. Soc. Exper. Biol. & Med.*, 31: 1125, 1934.
6. WATSON, B. P., SMITH, P. E., and KURZROK, R. Relation of the pituitary gland to the menopause. *Am. J. Obst. & Gynec.*, 36: 562, 1938.
7. SHEEHAN, H. L. Postpartum necrosis of the anterior pituitary. *Edinburgh M. J.*, 45: 13, 1938.
8. SEVRINGHAUS, A. E. Cellular changes in the anterior pituitary, with especial reference to its secretory activities. *Physiol. Rev.*, 17: 566, 1937.
9. HELLER, C. G., and HELLER, E. J. Gonadotropic hormone: urine assays of normally cycling, menopausal, castrated and estrin treated human females. *J. Clin. Investigation*, 18: 171, 1939.
10. VENNING, E. H. Further studies on the estimation of small amounts of sodium pregnandiol glucuronide in urine. *J. Biol. Chem.*, 126: 595, 1938.
11. FEVOLD, H. L., and HISAW, F. L. Interaction of gonad stimulating hormones in ovarian development. *Am. J. Physiol.*, 109: 655, 1934.



# DIAGNOSIS AND TREATMENT OF FUNCTIONAL UTERINE BLEEDING\*

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AS the term "functional" uterine bleeding would indicate, our concept of this disorder is that it is due to a functional derangement rather than to a structural lesion of one or other of the organs and tissues concerned in the menstrual cycle. The organs immediately concerned are the ovaries and the uterus, but beyond these, as we know, we must consider the possible rôle of distantly situated endocrine glands, especially the pituitary. As a matter of fact, most of what we have in recent years learned regarding the physiology of menstruation pertains to its endocrinology, so that it is not strange that in the explanation of abnormal menstrual bleeding it is the endocrine factors which have been most stressed.

And yet there is no doubt that functional bleeding is often due, in part at least, to derangements of other cogs in the menstrual mechanism. For example, we know very little as yet about the rôle of the uterine musculature, though it may be important. The perivascular interlacing arrangement of the uterine muscle makes it easy to understand that the degree of contraction or relaxation of these muscle bundles may have much to do with regulating the duration and amount of menstrual bleeding. However, it may well be that behind these variations lie variations in the quantitative balance between estrogen and progesterone, both of which have physiologic effects upon the uterine muscle.

Again, we must remember that menstruation is at bottom a vascular phenomenon, and that the rôle of the spiral arterioles of the endometrium, and probably of the vasomotor nerves, is an important one. The fundamental rôle of the

spiral arterioles has been beautifully demonstrated by the experimental studies of Markes upon endometrium transplanted to the anterior chamber of the eye, but here again the endocrine forces probably play the underlying rôle.

I mention these things merely to emphasize that we must not center our attention too exclusively upon the endometrium as a registering board of the endocrine dysfunctions which may bring about functional bleeding, important though such studies are. Not so many years ago it was the myometrium which was the cynosure of study in the attempt to explain "idiopathic" bleeding, and we may still be obliged to take a page from the book of Theilhaber and others, who in those days so valiantly championed the doctrine of "insufficiencia uteri" or muscle inadequacy of the uterus as a cause of this type of bleeding. The broad viewpoint, in other words, must include a consideration of all the links of the menstrual chain in the attempt to explain bleeding of this functional type.

The criticism may properly be made that we have tried to fit all cases of functional bleeding into the same dysfunctional mould. In a large proportion, it is true, the underlying disturbance seems to be a failure of ovulation, and a persistence of unruptured follicles beyond the normal span. The endometrium is therefore subjected to an abnormally persistent and excessive estrogenic growth influence, which in at least a considerable proportion of cases, is expressed in the histologic pattern which we call hyperplasia. The latter, it should be emphasized, is not the cause of abnormal bleeding, representing

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only an abnormal growth picture in the endometrium.

As a result of the see-saw functional relationship between the anterior pituitary lobe and the ovaries, periodic drops in the estrogen level occur in such a disorder, with an alternation of bleeding and non-bleeding phases. Since the corpus luteum is lacking in such cases, the characteristic of the endometrium is an absence of the secretory phenomena dependent upon progesterone, but not necessarily the presence of a hyperplasia of the full-blown, so-called Swiss-cheese pattern. There appears to be no parallel between the growth and bleeding propensities of the endometrium, so that in this group of cases one may find a genuine hyperplasia, or an endometrium corresponding to the earlier stages of the normal interval, or even an endometrium of rather atrophic type. Characteristically, however, one does not find secretory changes if the bleeding is due to the mechanism above described, as it is in the largest number of cases.

The fact remains that in a considerable group one may find an apparently normal type of endometrial cycle, with the normal sequence of proliferative and secretory phases. It is in this group that one must invoke other causal factors, such as a quantitative imbalance between the two ovarian hormones, or a disturbance in the spiral arteriolar apparatus, the vasomotor nerves, or uterine musculature. Concerning these factors, however, we know very little, and we are certainly still ignorant as to the nature of the liaison which must exist between them and the ovarian hormones. While, therefore, all these factors and many others must be considered in the explanation of functional bleeding, we must await further investigations before we can discuss all the possible mechanisms intelligently.

#### DIAGNOSIS

Speaking generally, the diagnosis of the functional nature of bleeding is justified

when thorough examination permits us to eliminate all evidence of structural or anatomic abnormalities in any of the pelvic organs. In the frequent bleeding of puberty and adolescence, for example, the functional nature may be assumed when the pelvic organs, on rectal examination, are apparently normal, with no evidence of the rather rare pathologic lesions, such as ovarian neoplasms, which may occasionally be found at this epoch. Few mistakes will be made by this simple method of elimination.

During the reproductive period, however, it is obvious that more direct evidence is necessary, because of the great frequency of intra-uterine pathology, such as retention of gestational products, polyp, submucous myoma, and carcinoma. Not only must extra-uterine lesions be eliminated by careful pelvic examination, but diagnostic curettage must ordinarily be done to eliminate intra-uterine disease. If microscopic examination shows no evidence of chronic endometritis, malignancy or other such lesions, and if there is no suggestion of such lesions as submucous myoma, one is justified in assuming that the bleeding is of functional nature.

The pathologic report on the endometrium in such cases is quite sure to be "normal endometrium" or "benign hyperplasia of the endometrium." If the former, the endometrium will most often be of the proliferative, non-secretory type, but it may be of a secretory variety, as I have already mentioned. If the report is of hyperplasia, the endometrium may grossly be enormously overgrown and polypoid, or it may be of moderate or even scanty amount. Similarly the hyperplasia may microscopically be of the frank Swiss-cheese pattern, or it may show only a moderate degree of hyperplasia. In these age epochs, therefore, the diagnosis is based upon the elimination of definite pathologic lesions, reinforced by the evidence of microscopic examination of the endometrium.

## TREATMENT

Aside from certain general measures which are more or less obvious, such as the treatment of the frequently associated secondary anemia, the treatment of functional uterine bleeding must depend upon two chief considerations, namely, the age of the patient and the importance or unimportance of preserving the reproductive function. Another important consideration which must always be borne in mind, especially in the treatment of young patients, is that the ovarian dysfunction responsible for the menstrual disorder is often a temporary one, and that there is a strong tendency in the majority of patients toward a reestablishment of the endocrine balance, after a bleeding career of variable and unpredictable duration.

It should be remembered, first of all, that the mechanism in most cases, especially those of the pubertal and adolescent type, is only an exaggeration of the anovulatory cycle so common at these periods of life. In other words, many young girls do not ovulate until they have menstruated for many months, or even several years, after menstruation has appeared. In such cases, menstruation may be essentially normal in amount and rhythm, but it may be irregular and profuse. Frequently the adjustment to normal periods takes place without any treatment at all, but, if bleeding is very profuse, the patient presents herself for medical care, and is promptly and properly diagnosed as having functional bleeding.

Bleeding may be so profuse as to necessitate transfusion, sometimes repeatedly. Curettage is rarely necessary for diagnosis, but is often indicated for its value in the immediate control of the bleeding. In cases of this group, as well as in those of older women in whom the desire for future child-bearing is an extremely important consideration, we have our chief field for organotherapy. Radiologists as well as gynecologists agree that radiotherapy should be used only as a last resort, even in carefully adjusted small dosage. In my experi-

ence such treatment has been necessary in only a very small proportion of cases.

Three chief groups of endocrine preparations are available for the organotherapy of functional bleeding, viz., (1) the pregnancy urine or A.P.L. substances, or, as we now consider them, the chorionic hormone preparations; (2) the progesterone preparations; and (3) the preparations of testosterone propionate.

The pregnancy urine preparations were first employed in the hope that they might bring about luteinization and progesterone production in the human. It should be remembered that when their use was first begun progesterone was not available for clinical use. While it is now known that these substances do not in humans bring about the hoped-for ovarian luteinization, the fact remains that in at least a proportion of the cases they do bring about cessation or lessening of the bleeding, so that they are still widely employed, sometimes with benefit, but often with disappointing results. When they are to be used, an average dosage varies between 200 and 500 units daily during the bleeding phases, though some use much larger doses.

When progesterone became available, it was but natural that it should have been resorted to in the treatment of a disorder in which absence of progesterone seems to be the outstanding endocrine defect. The results present about the same variations as with the pregnancy urine preparations, with sometimes striking effects on the bleeding, but in many instances little or no effect. The dosage has generally been far less than that known to be necessary for luteinization of a proliferative endometrium (60 to 90 rabbit units), varying ordinarily from 1 to 5 rabbit units (mg.) daily. The cost of higher dosage would be prohibitive to many patients. The smaller doses are perhaps not so illogical as they seem, for there is much reason to believe that the bleeding factor in the endometrium, whatever it is, is susceptible to much smaller hormonal doses than those required for its histologic transformation.

Finally, within the past two years or so, the androgenic hormone substances, chiefly in the form of preparations of testosterone propionate, have become very popular in the treatment of functional bleeding. There is still some uncertainty as to the effect of testosterone on the female genital cycle, but the evidence now available indicates that it exerts an inhibitory effect upon follicle ripening and the production of estrogen. Curiously enough, Hartman has shown that when given in the late secretory stage, it produces an accentuation of the progesterone effect.

When used in the treatment of functional bleeding of a periodic or menorrhagic type, testosterone should be given throughout the cycle rather than only after the onset of the bleeding. In milder forms of bleeding, even small doses of perhaps 10 mg. two or three times a week, are often highly effective. In the more severe types of bleeding large doses are required, though I rarely use more than 25 mg. three times a week.

Enthusiasm in the use of this preparation in women has been somewhat dampened by the publication of several cases in which such unpleasant sequelae as hirsutism and even voice changes have developed following this plan of treatment. In the moderate doses which I have employed in a rather large number of cases, I have observed no such effects. The fact remains, however, that if further experience should show that such unpleasant manifestations do occur with any frequency, most of us would be very circumspect in advising this plan of treatment even though these sequelae are of transitory nature. In the meantime I would advise the use of moderate dosage, rather than the large amounts which some have employed.

Finally, functional bleeding occurs most frequently of all in women of the menopausal age, using this adjective broadly as applying chiefly to the fifth decade of life. It is at this age period that more than one-

half of all cases are observed. In this large group the indications for treatment are quite different from those applying in younger patients.

Women of middle age have lived their reproductive lives, and the question of further child-bearing is usually of no importance. Their one desire is to be rid of the troublesome bleeding, and they are prepared for the menopause. Why bother such a woman with the uncertainties and annoyances of organotherapy when the problem can be so promptly and effectively solved by the abolition of ovarian function, as can be accomplished in all cases by adequate dosage of radiotherapy? This, therefore, is the rational plan to follow, and it represents one of the most valuable contributions of radiology in the field of gynecology. The use of radium or the x-ray for this purpose, however, should never be resorted to until the functional nature of the bleeding is established and other perhaps more serious causes eliminated by diagnostic curettage.

#### SUMMARY

There are certain cases of functional bleeding in which spontaneous readjustment of the endocrine balance takes place, with reestablishment of normal menstruation. When the bleeding is sufficiently profuse to impel the patient to seek medical advice, the proper management will depend chiefly upon the age of the patient and the importance of preserving the childbearing function. In young patients organotherapy will usually tide the individual over until the hoped for endocrine readjustment takes place, though curettage may be necessary for the immediate effect. In women of middle age in whom childbearing is no longer a consideration, the treatment in most cases should be diagnostic curettage to eliminate more serious lesions, followed by radiotherapeutic induction of the menopause.

# THE TREATMENT OF PRIMARY AMENORRHEA\*

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WHEN the menstrual flow has not made its appearance at the average age of puberty we speak of primary amenorrhea. Strictly defined, primary amenorrhea is presumptive evidence of a deficiency in the prepuberty sex impulse of the anterior pituitary gland. This deficiency may vary in degree from being nearly complete to just below the normal.

## ETIOLOGY

Physiologists generally agree that menstrual function depends upon the presence of a normally functioning anterior pituitary, a normally developed ovary capable of responding to the anterior pituitary gonadotropic hormones, and a normal uterus which reacts to the ovarian hormones, estrin and progestin. It is obvious therefore that primary amenorrhea may result from congenital deficiencies or from unfavorable conditions arising during the prepubertal period which adversely affect the anterior pituitary, the ovaries or the uterus.

Although the initiation and maintenance of ovarian function is chiefly dependent upon the pituitary, the development of the sexual organs and the appearance of the menstrual flow may be retarded by structural or functional deficiencies in other members of the endocrine system. While the thyroid, the adrenals, the pancreas and other ductless glands are primarily concerned with vital metabolic processes, there is evidence to show that the anterior pituitary gland reflects alterations in their functional status. It follows therefore that disturbances in one or more of these glands may unfavorably affect ovarian function by way of the pituitary.

Non-endocrine factors also may depress the organism as a whole and adversely affect pituitary and ovarian function. Among them are the constitutional and the general diseases of childhood, and the nutritional faults resulting from environment and diet. These remote but important causes have been somewhat obscured by the more spectacular revelations of the past decade which have focussed attention upon the endocrine glands. Although the glands that immediately control gonadal function undoubtedly play the leading rôle, it is equally true that any non-endocrine abnormality which unfavorably affects the general health of the individual may be reflected ultimately in the gonads.

## PROGNOSIS

The outlook in an individual case of primary amenorrhea depends not only upon the nature of the underlying abnormality but also upon its severity.

The general appearance of the patient gives some estimate of the difficulties that lie ahead. The prognosis is usually poor in the primary amenorrhea associated with retardation of the primary and secondary sex characters, for in such cases either congenital or developmental defects, or some prepubertal endocrinopathy are usually at fault. When, on the other hand, the condition is associated with normally developed sex characters, menstrual function may be spontaneously established or respond to treatment sooner or later.

Although pituitary insufficiency often involves both its sex and its growth-stimulating functions, exceptionally either one may be implicated alone. Consequently, normal or nearly normal growth

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may be associated with marked depression of gonadal function, difficult or impossible to influence, while, conversely, abnormalities of growth may coëxist with normal or only slightly retarded sexual development which may be quite amenable to treatment.

An important aid in determining the prognosis is a study of the prolactin and the estrin in the blood and urine. The presence of an increased amount of prolactin, if associated with an absence of estrin is an unfavorable sign, for it may signify an inherent defect in the ovaries which renders them refractory to stimulation. Where no increase in prolactin is demonstrable, the outlook is more or less favorable, depending on the amount of estrin present. If even small amounts can be detected, the outlook is fairly hopeful, for it indicates some degree of pituitary activity and the presence of a responsive ovary.

Where both the prolactin and the estrin tests are negative, it may be inferred that pituitary function is deficient. Whether in such cases the ovary is likewise inherently defective is difficult to ascertain.

A therapeutic test recommended by Hamblen involves the administration of a total of 3,600 mouse units of pregnant mare's serum over a period of four to six weeks. If at the end of treatment the uterine mucosa fails to show evidence of stimulation by one or both of the ovarian hormones it may be assumed that the ovaries are refractory. This test obviously presupposes the existence of a preparation capable of stimulating the human ovary.

It may be truthfully said that if we are able to remove handicaps to the general health and promote the well-being of the patient, as she grows older endocrine influences that have been dormant may be aroused and our purpose will be achieved.

#### DIAGNOSIS

Since there is such a multiplicity of influences which may underlie pituitary and genital dysfunction, there is scarcely any problem in the practice of medicine

that requires more painstaking and thorough study.

We note at the outset the gross evidence of endocrine disorders. Sometimes the endocrinopathy is stamped unmistakably upon the patient, as for example in cretinism, Fröhlich's syndrome or hypophyseal infantilism. But very often the gross evidence of pituitary, ovarian, thyroid, or adrenal dysfunction may be no more than suggestive and there may be such a combination of evidences that the clinical picture seems hopelessly confused and the predominating influence is a matter of speculation. Particular attention should be directed to the development of the primary and the secondary sex characters and the presence of statural anomalies or other endocrinopathic stigmata.

There are also special studies such as: anthropometric measurements to show the relative proportion of growth and sex impulses; basal metabolic estimations to measure the influence of the thyroid; sugar tolerance tests which may furnish some clue to the functional status of the pituitary; mapping the visual fields, and x-ray of the sella turcica to show the probable size of the pituitary gland and to disclose any sign of tumors of the gland or its environs; x-ray of the epiphyses to confirm the external evidence of too little or too much growth as well as the relative proportion between the growth and the sex impulses.

All of these procedures are preliminary to an actual study of the ovarian and the pituitary hormones in the blood and urine of which we have already spoken. In the normal case the ovarian hormone, estrin, is scarcely appreciable at the beginning of a cycle but gradually increases toward the end, the optimum time for its recognition being just before a period is due. In the primarily amenorrheic we have no basis for selection of this time. If no ovarian or pituitary hormones are discovered at the first examination or if the estimation is inconclusive, then weekly studies of the blood and quantitative estimations of

the total amount of estrin excreted in the urine over the full course of time usually occupied with a menstrual cycle will be needed. Only after such a search could one be certain that the reaction was completely negative. If the result is negative the studies should be repeated from time to time as the individual grows older since there may be a change in the endocrine function either naturally or as the result of treatment.

As no investigation may be considered complete without eliminating the possible non-endocrine causes, a thorough physical and pelvic examination as well as routine laboratory studies are of the utmost importance.

In the young amenorrhoeic no more of a pelvic examination should be made than is necessary to be sure that there are no gross pelvic anomalies. The development of the external genitalia, the distribution of the pubic hair and the size and form of the breasts are appreciable at a glance. The vaginal vault and cervix may be inspected with a Kelly cystoscopic speculum, the patient being in the knee-chest position. Bimanual palpation of the pelvic organs with a finger in the rectum will enable us to form some estimate of the development of the uterus and the ovaries. There is no use, however, in a searching pelvic examination at the beginning of the studies; it entails discomfort and may be otherwise objectionable in the conscious patient. Furthermore the palpable size and form of the pelvic organs may not give us a true estimate of their functional capacities. We find this out with greater accuracy at first by the estimate of hormones in the blood and urine and later by endometrial biopsy.

In obstinate cases we may examine the patient under anesthesia when close palpation of the adnexa is much facilitated. Exploration of the uterine cavity, curettage and hystero-graphy find their place in a complete search for structural anomalies and are of much value in determining the status of genital development.

#### TREATMENT

The treatment of primary amenorrhea necessarily entails an attack upon the underlying cause. Therapeutic measures, whatever they may be, should have a rational basis and should entail no danger to gonadal function. Prophylaxis is of the utmost importance. The parent and the family physician should be on the lookout for developmental faults and depressive states in young girls approaching the age of puberty. If the basic trouble is corrected before irremediable changes have occurred a permanent amenorrhea may sometimes be averted.

*Medical and Hygienic.* General medical measures directed toward the elimination of all subnormal manifestations, whether intimately or remotely connected with gonadal function, are indicated before any other plan of treatment. These may be effective in establishing normal menstrual function, particularly in cases in which some degree of sexual maturity has been attained.

This approach is specifically indicated in the amenorrhea due to debilitating diseases, or to any other fault of endogenous or exogenous origin which depresses the organism. Foci of infection, systemic disease, metabolic disturbances and other adverse influences should be eradicated.

*Dietetic.* The correction of nutritional faults is of prime importance.

The average normal individual selects his food according to his taste and this provides an adequate variety and amount of nourishment. In the amenorrhoeic girl there may be a faulty selection, ingestion or assimilation of food, either from conditions of physical and mental health or from economic situations or environment. Even when the individual is of normal weight and the food intake presumably adequate, the very fact that the menstrual function is lacking makes it possible that certain food essentials may be deficient.

In addition to the usual fruits, cereals, vegetables, meats and sweets of the table, the patient should add a selection of foods



especially rich in vitamins A, B and E, the ones which seem to be especially needed for the reproductive functions. The necessary vitamins may be given also in other forms as supplied by the trade.

In the *underweight* a high caloric diet rich in vitamins may be prescribed with due regard for the digestive and assimilative powers of the individual. The relative proportion of food elements including vitamins must of course be preserved. Sometimes the appetite and the assimilation of food are benefited by a daily injection of insulin, 5 units, just before the principal meal of the day, which should be rich in carbohydrates. Some restriction in physical and mental activities, definite periods of rest, fresh air and sunlight, natural or artificial, are conducive to successful results.

When anemia is an associated finding, iron, arsenic and liver extract, given with vitamin B complex, may be of much benefit.

By thus increasing the nutritional store of the body we may ensure an adequate supply of the basic substances from which the anterior pituitary and ovarian sex hormones are manufactured.

If these measures are all observed thoroughly, if a health promoting regime is prescribed, if the patient is lifted to the peak of physical condition and placed under the most favorable conditions of living, menstruation and some of the other evidences of puberty may make their appearance. Under such circumstances, of course, we may ask whether the essential endocrine background was not always there but required time and an improvement in general health for its development.

When the amenorrhea is associated with *obesity* an appreciable reduction in weight may be of value in establishing menstrual function; exactly how this is accomplished is obscure.

To effect a gradual loss of weight, a diet low in calories but one which insures an adequate supply of the basic food elements as well as essential minerals and vitamins, should be instituted. The coöperation of

the patient, her acquaintance with caloric values and an estimation of her weight every day will be conducive to success.

Besides limiting the caloric intake, some attention should be paid to water retention. The tissues of the obese often contain an excess of fluid. We may help by restricting the water intake and by promoting water elimination. The prescription of epsom salts or other saline cathartics twice a week and the administration of sodium citrate or other alkaline diuretic in concentrated form may be of value.

Massage, exercise and sweat baths will promote elimination by the skin.

*Endocrinologic.* We are quite immediately concerned with the therapeutic possibilities of improvement when the endocrine background is faulty. We must find a way of stimulating the production of sex hormones in the anterior pituitary.

There seems to be little doubt that the correction of functional disturbances of the thyroid may have a favorable influence upon gonadal and menstrual function. The empiric use of thyroid substance is considered by many observers one of the most effective methods available for the treatment of functional amenorrhea. The best results have been obtained in amenorrhea associated with obesity or with a depressed metabolic rate. Thyroid substance should be given a trial even when the basal metabolic rate is normal, for mild hypothyroidism may depress gonadal function without any other clinical evidence of thyroid deficiency. The manner in which the thyroid hormone aids in establishing menstrual function is not clear. Some believe that it acts by increasing the metabolic activity of the organism as a whole, and with it that of the ovary and its endocrine regulators.

The thyrotropic principle of the anterior pituitary gland deserves mention in the treatment of amenorrhea associated with thyroid hypofunction. At present there is not sufficient evidence to permit an estimate of the value of this substance in the human, and further clinical tests are neces-

sary. The possibility that protracted administration may create a refractory state due to the formation of antihormones which nullify its effect, must be kept in mind.

*Sex Hormones.* For the human being a really potent preparation of the sex hormones of the pituitary has not been found. The anterior pituitary-like gonadotropic hormones derived from the placenta or from pregnancy urine or blood may be administered as substitution products for the purpose of stimulating the endocrine and the ovogenic activity of the ovaries. Controlled studies with anterior pituitary gland extracts seem to show that little can be accomplished in the human with the preparations now available.

The spectacular effects produced with these preparations upon the gonads of lower animals have encouraged their extensive use for the treatment of amenorrhea associated with sexual immaturity or other manifestations of pituitary deficiency. While numerous reports lauding the efficacy of gonadotropic hormones have appeared in the literature, the few systematic attempts to ascertain their effect upon the human ovary leave us in doubt as to a stimulative effect.

*Pregnant Mare's Serum.* The most promising preparation thus far offered for clinical use is that derived from the serum of pregnant mares. Much attention is being given to this substance at the present time. Several observers have noted evidence of follicular growth and ovulation following its administration in the normally menstruating human and subhuman primate. Evidence that it is equally effective in patients with hypogonadism is limited and not completely convincing.

Hamblen has recently reported the case of a 17 year old girl with primary amenorrhea in whom mare's serum hormone therapy was employed after anterior pituitary gland extract had failed to elicit a response. A total of 1000 mouse units was given over a period of twenty days; this was followed after a lapse of one month by a total of

3,400 mouse units over a period of six weeks. During the course of treatment, enlargement of the ovaries and growth of the uterus was noted. At the end of treatment, endometrial biopsy revealed a pre-gravid type of endometrium and was followed two days later by bleeding. No further treatment was given but periodic bleeding occurred thereafter and rapid development of secondary sex characters took place.

A single case, though significant, justifies no definite conclusions as to the value of mare's serum therapy in primary amenorrhea. It must be noted that in Hamblen's patient a certain degree of sexual development had already taken place, as evidenced by the presence of axillary and pubic hair, and by the fact that the internal and external genitalia were of the juvenile rather than of the infantile type. In view of the fact that the patient was 17 years of age and therefore not yet beyond the limits of late puberty (known to occur as late as the twenty-first year), the possibility of spontaneous establishment of menstrual function must be taken into consideration.

Though Hamblen's experience does not by any means conclusively establish the efficacy of mare's serum hormone in primary amenorrhea, it certainly suggests that this substance is worth a trial.

It must not be forgotten that even a potent gonad-stimulating preparation will be of no value if the amenorrhea is due to some inherent defect which renders the gonads refractory to stimulation.

*Estrin and Progesterin.* The products of the Graafian follicle and of the corpus luteum may be used as substitution therapy in an attempt to effect the normal influence of these substances on the genital tract and the secondary sex characters.

The use of estrin or of estrin followed by progesterin in the treatment of amenorrhea is based upon the experimental and clinical observation that an adequate dose of these hormones will induce endometrial alterations similar to those seen during the follicular and the luteal phases of the

normal menstrual cycle. Upon completing a series of injections of estrin (total dose 1,000,000 international units over a twenty-one day period) followed by progestin (total dose of 35 or more rabbit units over a seven day period), there follows within a short time disintegration and bleeding from a pregravid type of mucosa.

Unfortunately the bleeding so induced has not been associated with any real improvement in gonadal function. It is probable that ovarian hormones have no direct stimulative effect upon the ovary. Some observers are hopeful that large doses of estrin may stimulate the gonads indirectly by way of the anterior pituitary and base their belief upon recent reports that rodents respond to intensive treatment with estrogenic hormones (for example 200 r.u. daily for twelve days) with ovulation and corpus luteum formation. Convincing evidence of a similar action in the human has not been found.

Some observers recommend the use of the estrogens (50,000 international units twice weekly) to develop and vascularize a hypoplastic uterus. Though undoubtedly effective for this purpose, little may be gained with such therapy in primary amenorrhea for the reason that if the uterus is hypoplastic the ovaries may be hypoplastic also. Unless their condition can be improved simultaneously, the induction of uterine growth is of no avail.

Not only are the estrogens of little value in such cases but they may actually do harm, for the huge doses required to stimulate uterine growth may further depress the already deficient ovary. We reluctantly conclude therefore that the ovarian hormones (estrin, progestin) although effective in stimulating endometrial growth and menstrual bleeding, are of no permanent benefit to the anterior pituitary or the ovaries. There is not much use in administering them just for the sake of producing uterine bleeding if a repetition of treatment is necessary for a second bleeding. Forcing one period or several periods by estrin and progestin does not seem to motivate either

the ovaries or the pituitary. The repeated use of substitution hormones in large dose may discourage and reduce the natural production. For the present therefore we do not employ them.

*Roentgen Radiation.* The Roentgen ray has been proposed for the purpose of directly stimulating the pituitary and the ovary. Although successful results have been reported by others from x-ray "stimulation" of the anterior pituitary we cannot be sure that we have seen any effect. It is admitted as a general proposition that the x-ray is depressing and not stimulating. A suggestion has been made that radiation increases the action of the anterior pituitary in the production of sex hormones by depressing certain factors inhibiting to the production of those hormones. We are skeptical about influencing the anterior pituitary favorably unless there is a demonstrable lesion of the pituitary or the midbrain regions.

We never use even the smallest dose of x-ray on the ovaries. Sometimes prompt and excellent results follow its use, but sometimes it has a disastrous effect. It is particularly hazardous in primary amenorrhea where the ovary is already deficient and even a very small dose may destroy the last vestige of function.

*Curettage.* Curettage as a surgical therapeutic procedure has often been abused. It is not advised in the young woman until the other measures of which we have spoken have been tried unsuccessfully. At a suitable time, however, it may be a wise procedure and it often serves a number of useful purposes. First of all, the opportunity of measuring the length of the uterine cavity and of determining the exact state of development of the uterus and adnexa may be possible only after anesthetizing the young patient. Such information is of course valuable if for no other reason than as a matter of prognosis. Secondly, an examination of the uterine scrapings gives a most reliable index of ovarian function. Thirdly, the mechanical irritation produced by dilatation of the

cervix and scraping the walls of the endometrial cavity may benefit the reproductive functions. This is in line with the observation that coitus as well as mechanical irritation of the cervix in the rabbit induces ovulation, and that there is improvement often in the menstrual function after marriage which apparently is due to the stimulating effect of sexual intercourse.

#### CONCLUSIONS

In patients with fair development of the secondary sex characters and without endocrinopathic stigmata, primary amenorrhea often yields to treatment.

The utmost and the closest attention should be paid to the general health as well as to the weight, the diet and the habits.

The interest and coöperation of the patient herself should be aroused. The nearer she can be placed to normalcy in every physical and mental respect the greater will become the capacity of her own endocrine glands to manufacture the hormones that she needs. Patience, persistence and the course of time will bring the desired results.

In patients with poorly developed sex characters or with endocrinopathic

stigmata, primary amenorrhea may be incurable.

Thyroid substance, especially in the obese and in the hypothyroid, is often of value; the thyrotropic hormone may be given a trial.

Estrin and progestin are not likely to be of permanent help and may do some harm.

The possibility of stimulating the anterior pituitary with the x-ray seems very remote; the success apparently attending its use by some observers may be explained on other grounds.

Roentgen ray treatment of the ovaries is some times followed by menstruation but it is a dangerous procedure; one never knows when it may destroy what little ovarian function there is and turn the scales against the patient.

Pregnant mare's serum may be tried on logical grounds since its effect more closely approaches that of the gonadotropic principles of the anterior pituitary than any other substance we possess.

Curettage affords us the most reliable index of ovarian function and may promote the development of that function by mechanical irritation. It should not be used until simpler means have failed and it becomes apparent that every therapeutic resource must be utilized.



# TREATMENT OF TRICHOMONAS VAGINALIS\*

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**L**EUCORRHEA is one of the commonest complaints among gynecological and obstetrical patients. From the symptomatic standpoint, it is usually the first to arise and the last to disappear. Davis,<sup>1</sup> in examining 1000 female patients, found that 33 per cent had some type of discharge. This is about the percentage in my practice and in the gynecological clinic of the Jefferson Davis Hospital, Houston, Texas. *Trichomonas vaginalis* is one of the most common causes of leucorrhea, but had been overlooked until our research at the University of Texas School of Medicine.

The first case of *trichomonas vaginalis* reported in the United States was by George Dock<sup>2</sup> in Galveston, Texas, where most of this research was carried out. The first papers on *trichomonas vaginalis* were reported by Donne<sup>3</sup> in 1837 and later ones by Kunstler<sup>4</sup> in 1893 and 1894, by Benson in 1912, DeLee<sup>5</sup> in 1920, Reuling<sup>6</sup> in 1921, Hegner<sup>7</sup> in 1925, Bland and Rakoff<sup>8</sup> in 1932. Since that time many American authors, such as Hesseltine,<sup>9</sup> Drabkin,<sup>10</sup> Buxton and Shelanski,<sup>11</sup> and the author<sup>12</sup> have added to the literature.

*Incidence of Trichomonas Vaginalis.* In 1932 at the John Sealy Hospital, Galveston, 500 consecutive women coming to the outpatient clinics of the hospital were examined. There were 187 positive cases of *trichomonas vaginalis*, a percentage of 37.4. There were 300 negro and 200 white females; 46.3 per cent of the negro females, and 24.0 per cent of the white females harbored the organism. These patients ranged from 11 to 52 years of age. The largest percentage of positive cases of *trichomonas vaginalis* lay between the ages of 19 and 33 years with the largest single group at 23.

According to the author's statistics, based upon the examination of over 10,000 women, trichomoniasis was present in 37.5 per cent of the gynecological and obstetrical patients in Galveston, Texas, a seaport, and in only 27 per cent of the same class of patients in Houston, Texas, 52 miles inland. The author has examined more than 25,000 female patients for *trichomonas vaginalis* during the past eight years and the percentage of patients found positive was 25.5 per cent.

*Urinary Infections.* Flashkamp<sup>14</sup> found *trichomonas vaginalis* in the urine in one out of 250 patients examined, and Sayer<sup>15</sup> in 27 per cent of 212 patients examined. Sayer believes the bladder to be the normal habitat for *trichomonas vaginalis*. In our resistant and obstinate cases, we find *trichomonas vaginalis* more often in the bladder. Whenever one fails to cure trichomonas vaginalis by the routine method, such as floraquin and vinegar douches, then at the same time as the vagina is treated, the bladder is irrigated with boric acid followed by the instillation of argyrol.

*Signs and Symptoms.* The patient usually complains of a discharge or "whites" with an itching and burning, or chafing, of the external genitalia and inner aspect of the thighs. No other discharge produced by the vaginal mucosa and no other microorganisms besides the *trichomonas vaginalis* causes a scalding sensation of the vagina, vulva and perineum.

The discharge is usually thin and creamy in color, but it may be thick and yellowish. At times it is difficult to distinguish trichomonas infection from gonorrheal infection. The discharge of *trichomonas vaginalis* usually resists all types of treatment, but it may sometimes be checked by

\* From the Department of Gynecology, Jefferson Davis Hospital.

simple douching, or with one of the common antiseptics on the market advocated for this protozoan infection. However, the discharge soon recurs as profusely as before. There is an increase in the discharge and burning at the beginning and more so at the end of menstruation, with less burning and itching during the period.

Some patients have as their chief complaint burning on urination, others dyspareunia, still others difficulty in walking due to the marked scalding of the exposed surfaces of the thighs. The most common complaint is a discharge that causes an itching of the external genitalia. In our study of more than 5000 cases of pruritus vulvae in the gynecologic clinic, 90 per cent were due to trichomonas vaginalis,  $\frac{1}{2}$  per cent to monilia albicans of the vagina, and the rest to various rare causes.

On examination of the vulva one sees an excess of discharge if the patient has not taken a douche within the past hour. In some cases there is very little discharge. In most cases the discharge will run out of the vagina on separation of the labia. In some cases many scratch marks give evidence that the patient has had a great deal of itching. There may or may not be an associated cervical discharge.

In the acute cases of trichomonas vaginalis, there is a diffuse reddening of the vulva, vagina, or cervix, similar to that noted in any other acute vaginitis.

In the chronic cases of trichomonas vaginalis there may be the so-called "colpitis granulosa," "strawberry vagina" or "salt and pepper vagina." This is characteristic of trichomonas vaginalis, we believe. In eight years of leucorrhea research, we have not seen it in any other vaginal conditions.

**Diagnosis.** The patient is instructed not to take a douche for twenty-four to forty-eight hours before coming to the office for an examination for the cause of her leucorrhea. If it is her first visit, a smear is made, even if she has taken a douche and a microscopic examination for organisms made. She is instructed to return

the next day without douching for a second vaginal smear study.

Two cotton applicators are inserted into the posterior fornix of the vagina before any vaginal or speculum examination is made. The two applicators are placed in 0.5 c.c. of ordinary tap water in a test tube, and are turned around several times in the tube in order that the secretion may be loosened somewhat. A thick smear is then spread across the entire length of a clean slide. Movement is looked for under low power. If the patient has not taken a douche and if lubricating jellies have been omitted, one will observe in a positive case of trichomonas vaginalis many organisms moving around. For more detail the higher power of the microscope may be used.

**Physiology of the Vagina.** The physiology of the normal vagina should be considered before the logical approach to treatment may be arrived at. We have outlined treatment in this paper after an exhaustive study of vaginal pH, epithelial cell height, vaginal bacterial flora, glycogen contents of the epithelial cells, and the way glycogen is broken down into acids in the vagina.

The vagina is a tubal organ which varies in length and size. It is an organ where sperm are deposited, a birth canal, and conveys menses from the cervix to the introitus.

At the introitus, there is a normal drying mechanism of the secretion that passes by osmosis through the mucosa of the vagina and of the secretion that comes from the cervix. Most of the vaginal secretion is produced in the vagina, but a small amount of it comes from the cervix. If the secretion is in excess of that which can be normally dried at the vulva, the patient usually complains of a discharge.

The reaction of the normal vagina is acid, as tested with nitrazine paper (Squibb), Hellige, Wulff or the electrometric method. The pH varies from 3.9 to 4.4. We have tested pH in over 5000 vaginas in our clinic; for all practical purposes the normal pH may be considered about 4.0.

In view of these observations, all medication should be of pH approximately 4.0 or below. Precautions should be taken not to produce a pH so low that the vaginal mucosa will be burned. I have found that a pH of 2.9 is most suited for douches, and that sugars, such as glucose, maltose, saccharose, lactose, or a combination of the four, are of great benefit in the treatment of most vaginal infections.

A stained biopsy of the normal vaginal mucosa shows about forty-five to fifty-five cell layers in height. Sections of normal vaginal mucosa stained with Best's carmine stain or other glycogen staining methods, show an abundance of glycogen granules in the epithelial layers. The upper layers of the vaginal epithelial cells are well vacuolated and these vacuolated areas are receptacles for glycogen which is picked up from the blood by the vaginal epithelial cells. The glycogen is broken down into glucose and finally into lactic acid, which is the normal acid of the vagina. This is carried out by enzyme action and the action of Döderlein bacilli. Other organic acids are also produced.

The application of Lugol's solution to the normal vaginal mucosa produces a deep mahogany color, due to the action of iodine on glycogen. If there is a loss of glycogen, no change in color results; if there is a decrease in glycogen, there is decrease in the intensity of the mahogany color.

In infections of the vaginal mucosa there is a depletion or almost complete loss of glycogen, with less mahogany color formation and less acid reaction. In an infected vagina there is a positive decrease in the amount of glycogen stored in the epithelial cells.

A fresh or stained smear from a normal vagina shows many fat, stick-like organisms (Döderlein bacilli) and many large clumped epithelial cells with small nuclei. The epithelial cells stain normally. There are few pus cells or none at all.

If a smear from an infected vagina is made, whether the infection is due to trichomonas vaginalis or some other organ-

ism, few, if any, of these Döderlein bacilli are seen. We will also see many shapes, forms, and kinds of micro-organisms, such as streptococcus, staphylococcus, and colon bacillus. The epithelial cells do not take the stain so readily and the epithelial cells are no longer in clumps, but are broken up into fragments. It may be said, then, that in an infected vagina there is a mixed vaginal flora, with a positive decrease in the Döderlein flora normally present.

There is, therefore, a state of deficiency of four physiologic elements: (1) hypo-acidity; (2) hypo-glycogen; (3) hypo-epithelium; and (4) hypo-Döderlein.

*Acidity and Alkalinity and Growth of Vaginal Micro-Organisms.* To substantiate the above research, eight cases of acute vaginitis with a very foul malodorous discharge were surveyed in an experiment. The patients were told not to take douches, to omit coitus, and not have any vaginal treatment for two weeks. External plain water washes were allowed. By sterile technique, all the vaginal secretion that could be collected from the vagina was placed in 0.5 c.c. of warm sterile water in a sterile test tube. From this solution a smear was made on agar of a pH of 2.8, 3.6, 4.4, 5.4, 5.5, 6.0, 7.0, 7.2, 7.6, and 8.0.

TABLE I

Case	pH of Vaginal Secretion	pH of Media and Growth of Vaginal Micro-Organisms										Broth and Agar Control
		8.0	7.6	7.2	7.0	6.0	5.5	5.4	4.4	3.6	2.8	
1	6.8	8x	8x	6x	5x	3x	3x	2x	0	0	0	7x
2	6.0	8x	8x	5x	3x	3x	0	0	0	0	0	8x
3	6.8	8x	7x	5x	4x	3x	0	0	0	0	0	8x
4	6.5	8x	8x	6x	4x	3x	3x	0	0	0	0	8x
5	5.9	8x	8x	6x	4x	3x	3x	0	0	0	0	8x
6	6.0	8x	8x	8x	4x	3x	3x	2x	0	0	0	8x
7	6.6	8x	8x	5x	4x	3x	3x	2x	0	0	0	8x
8	6.3	8x	8x	5x	4x	3x	3x	2x	0	0	0	8x

0 = no growth.  
8x = profuse growth.  
2x = slight growth

Bacterial growths were most abundant at a pH of 7.6 and 8.0 and as the pH became more acid, the bacterial growth became less and less. There was no growth at a pH of 5.5 in two cases, 5.2 in four cases, and 4.4 in

all cases. Controls were used and growths were most abundant at pH of 7.6 and 8.0. There were no growths at a pH of 4.4 or below. Staphylococcus and colon bacillus did not grow at a pH of 5.0 or below. (Table I.)

were instructed to insert one dose of this jelly into the vagina at night and in the morning. Vaginal cultures were made after jelly of different pH was used in the vagina from three days to six months. The results were similar to those obtained when the

TABLE II

Drug	Amount of Drug	Amount of Water	Microscopic Results	Clinical Results	pH
Sodium perborate....	3 heaping teaspoonfuls	Quart tap water	No death	Poor	10.0
Borax.....	3 heaping teaspoonfuls	Quart tap water	No death	Not good	9.0
Sodium bicarbonate..	3 heaping teaspoonfuls	Quart tap water	No death	Not good	8.0
Dilute sodium hydroxide.....	.....	In tap water	No death	Not good	8.0
Magnesium sulfate...	3 heaping teaspoonfuls	Quart tap water	No death	Not good	7.5
Sodium chloride.....	1 cup	Quart tap water	Stops mobility immediately. No death.	Fair, does not destroy trichomonads	7.4
Silver picrate.....	4 gr.	5 c.c. tap water	No death	No death with 4 or less gr.; 5 gr. death. Fair.	7.3
Potassium permanganate.....	3 tablets	Quart tap water	Death	Fair	7.3
Boric acid.....	3 heaping teaspoonfuls	Quart tap water	No death	Not good	6.1
Caprokol.....	1 drop	In vaginal smear on slide	No death	Not good	5.9
Anayodin.....	8 c.c.	In tap water	No death	Not good	5.8
Verazeptol.....	1 teaspoonful	Quart tap water	No death	Not good	5.8
Lugol's solution.....	2 heaping teaspoonfuls	Quart tap water	Death	Good	5.6
Dilute HCl.....	.....	In tap water	Death	Good	5.0
Orthogynol.....	1 drop	In vaginal smear on slide	Death	Good. Death immediately	4.5
Acetarsonone.....	1 gr.	5 c.c. tap water	Death	Good	3.9
Alum.....	1 gr.	5 c.c. tap water	Death	Good, but dries vagina too much	3.6
Vinegar.....	5 tablespoonfuls	Quart tap water	Death	Good	3.5
G. C. douche powder	3 heaping teaspoonfuls	Quart tap water	Death	Good	3.0
Floraquin.....	¼ tab.	5 c.c. tap water	Death	Death immediately.	2.9
Acetylsalicylic acid...	5 gr.	5 c.c. tap water	Death	Good	2.9

NOTE: Nitrazine paper (Squibb) is ideal to determine the pH of vaginal secretion and douches.

*Jelly at Varying pH.* Sixteen other patients with acute vaginitis and foul malodorous discharge were given jelly at a pH of 2.0, 2.5, 3.5, 3.7, 4.0, 4.5, 4.6, 4.7, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, and 9.0. The patients were instructed not to take douches, to omit coitus, and to have no type of treatment in the vagina. They

vaginal micro-organisms were cultured on media at different pH, as given above.

Regular ortho-gynol jelly was used in sixty patients with nonspecific infections and found to be efficient clinically, as well as when tested culturally and under the microscope in the laboratory. The jelly is soft and easily applied and was found



to be satisfactory for the treatment of nonspecific vaginal infections in 89 per cent of the cases.

The first work along this line was done by Döderlein in Germany. Then came the work of Cruickshank and Sharman of England, followed by our work in Houston and Galveston. Since my results have been published, other investigators have made similar reports.

Acidity is the most important factor in the treatment of trichomonas vaginalis and in any vaginal infection. Those who are at present using antiseptics without regard to the pH of the drug would find their results greatly improved if an acidifying agent were used.

I have used almost every drug advocated for the treatment of trichomonas vaginalis, and found that they all give approximately the same results unless they have a low pH. Most drugs advocated for trichomonas vaginalis gave us a 70 to 80 per cent clinical cure in from three to six months.

Most of these drugs, however, have never been tested directly in contact with the trichomonas under the microscope. We have attempted to correlate the microscopic and clinical results, after testing the pH of the solutions to determine whether there was any relationship between the clinical results and the findings under the microscope, and between the pH and the death of the trichomonas vaginalis.

The following drugs were tested: silver picrate, floroquin, borax, vinegar, sodium chloride, sodium bicarbonate, sodium perborate, potassium permanganate (10 gr.), boric acid, and a gonorrheal douche powder containing alum, zinc sulfate, menthol, and boric acid. Magnesium sulfate, alum, acetarsone, acetylsalicylic acid, ortho-gynol jelly, dilute hydrochloric acid, verazseptol, caprokol, anayodin, dilute sodium hydroxide, and Lugol's solution were also tested. (See Table 1.)

Death of trichomonas vaginalis usually occurs when the pH is 5.6 or lower. As the alkaline side is approached, the drug has less effect. At pH 8.0 and 9.0 the trich-

omonads were motile and cell division took place. They lived longer and were more motile in an alkaline medium. Thus trichomonas vaginalis can live easily in the cervical canal, which has a pH of 7.2 to 9.0. I am of the opinion that the organisms pass into the cervix and live. This is one of the reasons for recurrences, as, after treatment is discontinued, they emerge from the cervix and reinfect the vagina. They also occur in greater numbers and more frequently in urine which is alkaline or near the alkaline side. Trichomonas vaginalis can live and multiply in most normal or abnormal urine of the bladder. In many resistant cases I have found the recurrence to be due to reinfection from the bladder.

In the male urethra, under the prepuce, and in the prostate, the secretion has an alkaline pH of 7.2 to 7.5. It is possible for the trichomonas to live there and reinfect the partner at coitus. I have reported thirty-eight such cases.

*Treatment.* After a positive microscopic diagnosis of trichomonas has been made, or whenever a patient complains of a foul malodorous discharge that causes an itching or burning of the external genitalia, and in all vaginal infections, the following treatment is advocated: the vulva, vagina and perineum are gently washed with vinegar water (five tablespoonfuls in two quarts of water) and dried. One to 2 drams of floroquin powder are then blown into the vagina or four to eight floroquin tablets are inserted, encircling the cervix, with a small plug of cotton inserted at the introitus. The patient is given a prescription for twenty-four floroquin tablets, one to be inserted each morning and one each night. Instructions should be given not to douche during this period. Perineal pad and external washes are to be used as necessary. After twelve days, vinegar water douches (5 tablespoonfuls of vinegar to 2 quarts of water) are to be taken twice a day between and during the next three menstrual periods and up to the fourth menstrual period. Acetic or lactic acid (5 per cent) may be used. At the end of the fourth

menstrual period a fresh vaginal smear is made for trichomonas vaginalis, and if found negative the patient is pronounced cured. If the smear is positive, the treatment is resumed.

Following each menstrual period for two to five days, one floraquin tablet is inserted morning and night with vinegar douches as needed for cleanliness.

The patient is instructed to insert two floraquin tablets as soon as the slightest itching or discharge returns and to insert one tablet night and morning for six days.

The patient returns twice each week for two weeks for observation as to how the infection is progressing. Floraquin powder insufflations are used as needed.

In acute cases of trichomonas vaginalis, pruritus vulvae, or vaginitis with a great deal of tenderness, 1 to 2 drams of floraquin powder are blown into the vagina every day until the soreness is gone. Due to the soreness of the vaginal tract an acid jelly (ortho-gynol) can be inserted night and morning as a home treatment. After the acute stage has subsided, one floraquin tablet is inserted night and morning as the home treatment.

In 400 cases of trichomonas vaginalis in private practice and over 4,000 charity cases at the Jefferson Davis Hospital, 94 per cent were cured by this method. Antiseptics and the various unscientific procedures are no longer used or advocated. We now have a sound scientific method which gives us excellent results.

Shelanski and Buxton advocate silver picrate, but it has an alkaline pH. I have seen 400 private patients for the treatment of trichomonas vaginalis and 98 per cent of them had had from one to several courses of treatment with silver picrate, and all were still positive for trichomonas vaginalis. Silver picrate causes in many cases a peeling of the vaginal mucosa of the wife and of the penis of the husband. We do not advocate any alkaline preparations. Kaldor<sup>13</sup> suggested concentrated salt douches. This has been found to be no

more efficient than the ordinary drugs or antiseptics already advocated.

We have used the lactose citric tablet but found that too many patients could not stand the smarting and burning from the citric acid. Tartaric acid does not produce the smarting and burning and is advocated instead of citric acid. This preparation has a pH of approximately 3.5. If one ascertains that the pH of the powder, solution, jelly or tablet to be used is lower than 5.6, a higher percentage of cures will result.

Hibbert's streptococcus subacidus vaccine has been used in fifty patients, two of whom obtained relief from their itching. The itching returned, however, in two to three months.

#### CONCLUSIONS

1. Solutions, tablets, powders or jellies of pH 5.0 or lower should be used. Drugs with pH above 5.0 should not be used.

2. Vinegar (5 per cent acetic acid), acetarsone, Lugol's solution, glucose-lactose pH 2.9 tablets and powder (floraquin), alum, ortho-gynol jelly, lactic acid, or any similar solution of pH 5.0 or less is worth using.

3. The above drugs were destructive to all the abnormal microorganisms of the vagina and did no harm to the normal vaginal organisms.

4. Clinical results corresponded directly to the pH in the clinical cases of more than 4,000 women treated with the drugs listed above during the last seven years.

5. Silver picrate pH 7.3 is not advocated. Ordinary dry sieved cornstarch or kaolin in powder form, accompanied by vinegar douches as the home treatment, will give better results. These are more reasonable in cost also.

6. In a high percentage of cases it is the acidity of the drug that destroys vaginal micro-organisms rather than its specific bactericidal action.

7. One or 2 drams of floraquin powder are blown into the vagina or four to six tablets of floraquin are inserted at the first visit. The patient is instructed to insert one

tablet night and morning with no douches for twelve days. Only external washes are allowed for cleanliness. Vinegar douches, are taken three times a day during the menses.

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#### REFERENCES

1. DAVIS, C. H. Leucorrhea with special reference to trichomonas vaginalis. *Am. J. Obst. & Gynec.*, 18: 196, 1929.
2. DOCK, G. Trichomonas as a parasite of man. *Am. J. M. Sc.*, 111: 1, 1896.
3. DONNE, A. Animalculae observed in purulent matter and in the secretions from the genital organs of men and women. *Compt. rend. Acad. d. sc.*, 3: 385, 1836.
4. KUNSTLER, J. Microscopic examination of the urine of a patient with chronic pyelitis. *J. de med. de Bordeaux*, 13: 249, 1893.
5. KUNSTLER, J. Trichomonas vaginalis. *J. de micro.*, 8: 317, 1894.
6. DELEE. Trichomonas vaginalis vaginitis. *Illinois M. J.*, 37: 186, 1920.
7. REULING, F. Morphology of trichomonas vaginalis. *Arch. protistenk.*, 42: 347, 1921.
8. HEGNER, R. Trichomonas vaginalis Donne. *Am. J. Hyg.*, 5: 302, 1925.
9. BLAND, P. B. Leucorrhea: its significance and treatment. *South. M. J.*, 25: 17, 1932.
10. HESSELTINE, H. C. Evaluation by controlled series of vaginal trichomoniasis therapies. *J. A. M. A.*, 109: 768, 1937.
11. DRABKIN, C. P-carbamino phenyl arsonic acid in treatment of trichomonas vaginalis vaginitis. *Am. J. Obst. & Gynec.*, 33: 846, 1937.
12. BUXTON, R. VON L., and SHELANSKI, H. A. Trichomonas vaginalis vaginitis; incidence, diagnosis and treatment with silver picrate. *Am. J. Obst. & Gynec.*, 33: 842, 1937.
13. KARNAKY, K. J. Trichomonas vaginalis. *Urol. & Cutan. Rev.*, 38: 174, 1934. *M. Rec. & Ann.*, 28: 394, 1934. *Texas State J. Med.*, 29: 662, 1934; 30: 48, 1934; 30: 606, 1935. *M. Rec. & Ann.*, 28: 635, 1934.
14. KARNAKY, K. J. Leukorrhea: trichomonas vaginalis and monilia albicans. *M. Rec. & Ann.*, Sept. 1935.
15. KARNAKY, K. J. Trichomonas vaginalis and monilia albicans as causes of leukorrhea. *South. M. J.*, 28: 796, 1935.
16. KARNAKY, K. J. Trichomonas vaginalis vaginitis; pathognomonic lesion and pathogenic findings in 4000 cases. *Texas State J. Med.*, 32: 803, 1937.
17. KARNAKY, K. J. A rare case of trichomonas intestinalis in stool and trichomonas vaginalis in the bladder and vagina of a ten month old child. *South. M. J.*, 29: 939, 1936.
18. KARNAKY, K. J. Bodo urinarius (caudatus) in urine, often called trichomonas vaginalis. *Urol. & Cutan. Rev.*, 40: 11, 1936.
19. KARNAKY, K. J. Normal physiological douches. *South. M. J.*, 30: 69, 1937.
20. KARNAKY, K. J. Leukorrhea; its causes and treatment. *M. Rec. & Ann.*, June 1938.
21. KARNAKY, K. J. Vaginal leukorrhea; its causes and treatment. *Radiol. Rev.*, 208, 1938.
22. KARNAKY, K. J. Why does trichomonas vaginalis recur? Report of 38 cases. *Urol. & Cutan. Rev.*, 42: 11, 1938.
23. KALDOR, J. J. A. M. A., 105: 105, 1935.
24. CURTIS, A. H. Textbook of Gynecology and Obstetrics, pp. 429 and 432. Philadelphia. Saunders.
25. DAVIS, G. H. Textbook of Gynecology and Obstetrics, vol. 2, p. 79. Hagerstown, 1932. Prior.
26. Yearbook of Obstetrics and Gynecology, pp. 338, 443, 447, 1936; pp. 319, 438, 446, 452, 1937; pp. 420, 428, 1938.



# THE MENOPAUSE

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THERE are various types of true climacterics: the natural, the radiologic, and the surgical. The natural menopause may be subdivided into the precocious and the usual; the latter occurring at or about the age of 47. The radiologic menopause can be brought about by intrauterine radium or the use of the Roentgen ray, both of which destroy the function of the ovaries. The surgical menopause is the quickest and of course is the most complete. In the natural or radiologic menopause ovarian tissue is still present and it is possible to imagine a follicle seemingly inactive being reactivated. Complete death of all follicles may not occur and at a later period menstruation may start over again.

## DIFFERENTIAL DIAGNOSIS

The menopause, true ovarian failure, can easily be confused with another type of cessation of the catamenia, that is, the amenorrhea due to pituitary failure. In this type of amenorrhea absence of hot flashes is a characteristic clinical symptom. The possibility of pituitary failure must be considered in all cases of amenorrhea. It can be differentiated in the laboratory from ovarian failure by the absence of the follicle stimulating hormone in the urine. A low 17 ketosterone determination\* in the urine in addition to absent follicle stimulating hormone is practically confirmative of pituitary failure. Debilitating disease is frequently accompanied by ovarian hormone suppression, but this is not the true

menopause. Toxic thyroid disease and myxedema are often associated with amenorrhea. Lack of ovarian development is accompanied by lack of menstrual function; however, this should not be interpreted as the menopause but rather as a primary ovarian amenorrhea. The menopause means cessation of menstruation following failure of a once active ovarian function.

## SYMPTOMS

The symptoms of all menopauses are similar. Usually there is an occurrence of hot flashes, though many patients never seem to have had them. Dizziness is frequent, as are night sweats and depressions. Hot flashes may commence in any region of the body from extremities to face but usually end up by causing a marked facial vasomotor disturbance. Patients have a sensation of suffocation and oppression, often rush to a window, or begin to fan themselves. It is extraordinary how infrequently hot flashes are noticed in friends, yet each patient is violently conscious of her own flashes and is embarrassed by them. This phenomenon may be very infrequent, frequent, or very frequent—ranging from one to thirty each twenty-four hours. Night sweats are common and cause concern because of the possibility of contracting cold or pneumonia. It is necessary for certain patients to get up out of bed and change their night clothes because of the excessive perspiration that has occurred with the flashes.

Dizziness is a very common symptom and is often diagnostic of ovarian failure. This symptom is very distressing because it causes a certain amount of insecurity. Some women feel unsafe driving a car or

\* The 17 ketosterone determination is a colorimetric procedure used as a measure of secretion of the androgen-like substance of the adrenal cortex. Therefore lack of it is interpreted as indicating anterior pituitary failure, at least of the hormone that stimulates the adrenal cortex.

crossing the street. Depression is usual and may range from a feeling of blueness to a deep and melancholy depression.

Personality changes occur; the simple sweet woman may become aggressive and domineering and the masculine woman may become sensitive and kindly. Some women lose all libido, and yet others have an enormous increase in sex desire. Occasionally with loss of normal sex feeling abnormal desires commence.

Physical characteristics may change in some instances; occasionally a woman becomes gross and obese. Increase of weight is often due to laziness and over-indulgence following surgery or radium. The patient never recovers her pride and uses her operation and artificial menopause as an excuse to avoid excessive activity. And she overeats. Abnormal growth of hair is not common, but with lack of estrin and a comparative increase in androgen this may be expected.

All sorts of changes may occur but we all know that most climacterics are not violent, depressive, masculine, or productive of grossness, especially when the great number of gentle, sweet, old ladies is considered. Increased ability, energy, and a delight at relief from "the curse," should assure most women that the menopause holds no terrors. A perfectly natural state, a release from fluctuating glandular waves, the menopause should be and in most instances is the most comfortable time of a woman's life.

#### PATHOLOGY

In the menopause certain fundamental changes occur. The primordial follicles and ova vanish because they are all used up or disappear because of some unknown reason. Graafian follicles fail to develop and the ovary becomes fibrous. The stroma changes from a vascular, active connective tissue to a tough fibrous or even hyaline type. The ovary finally is a small wrinkled organ without signs of activity.

Following cessation of ovarian function the breasts atrophy as there is no longer

any active ovarian stimulation. The breasts take on a characteristic lumpy, doughy feel characteristic of the menopause. The uterus atrophies and is inactive. It resembles the juvenile uterus, with the cervix the same length as the fundus. There is an increase of connective tissue and decrease of smooth muscle. The endometrium shrinks and the glands that are left lie parallel to the uterine muscle rather than perpendicular to it. Frequently but one layer of cells lines the endometrial canal. The cervix becomes smaller and often more pointed. At this time a scarred cervix may become very narrow and any secretions from the endometrium may lack drainage and pyometrium may develop. The vagina atrophies and large round cells or typical menopause cells are found on vaginal smears. The lack of succulence and vascularity of the mucous membrane of the vagina is conducive to infection and vaginitis often occurs, followed by adhesions, a cause of partial obliteration of the vagina. The vulva also changes, the skin becomes dry and thin. Sometimes the clitoris is involved in cicatrices followed by infections in the region of the prepuce. Vulval atrophy may be severe, and subsequent infection may be responsible for leucoplakic vulvitis, the end result of which may be typical kraurosis. The urethra is involved in the vaginal atrophy and may become tube-like and narrow. Incontinence and frequency of urination may follow. The skin about the anus may become tough and fibrous and cracks and fissures and small hemorrhoids may result.

The pituitary gland hypertrophies and secretes an excess of follicle-stimulating hormone. Other glands may have an increase of secretion but this increase may be only relative. It is well known that thyrotoxicosis and myxedema often occur at the time of the menopause. Hypertension is common at this time and a cause for it may be found in the adrenal medulla, which may oversecrete and cause vaso-motor changes. If masculinization occurs it may be due to a relative increase of

androgen or to an actual increase in secretion of the adrenal cortical hormone.

The menopause caused by cessation of ovarian function is usually compensated for by the end of the first year. The greatest number of women go serenely on, but others have severe and devastating difficulties and some are changed permanently.

#### BIOLOGIC CONSIDERATIONS

In studying the menopause biologically two findings are definite. There is nearly a complete absence of estrin; and an increase in the follicle-stimulating hormone (usually called F.S.H.) of the anterior pituitary gland. In many patients with menopause symptoms some small amount of estrin can be demonstrated. The source from which it comes is not quite clear, but it is possible that the adrenal cortex may be responsible, or there may be some metabolic breakdown of androgen or a change in cholesterol metabolism. This amount of estrin is very small and it does not affect the menopause symptoms to any great extent. It is conceivable, however, that certain women who have few symptoms may be among those who have large amounts of extra-ovarian estrin. F.S.H. is definitely increased and certain investigators believe that the seriousness of menopause symptoms is in proportion to the amount of this hormone. It is true that the presence of estrin in the urine of menopause patients does not necessarily mean a lessening of symptoms, but lowered amounts of F.S.H. are of great importance. Pituitary failure may be considered a cause of amenorrhea or suspected menopause when there is no F.S.H. in the urine, for in ovarian failure it should be present. If the determination of the 17 ketosterone, which is indicative of androgen in the urine is low, it can be considered as indicating lowered adrenal function. This probably is indicative of lowered pituitary function and if, in addition, in cases of amenorrhea there is no F.S.H. in the urine, pituitary failure is probably present.

The presence or absence of F.S.H. differentiates most cases of amenorrhea, but

determinations of 17 ketosterone and of estrin help point out the responsible gland.

#### TYPE OF MENOPAUSE

The natural menopause may be divided into two types, the precocious and the normal. The menopause in young women is considered precocious. In this type the ovary fails or atrophies and typical menopause symptoms commence—hot flashes, etc. F.S.H. will be positive, estrin practically absent. This type should respond to treatment and the hot flashes cease. In such cases the ovaries are usually very small and atrophied and there is a lack of primordial follicles. The treatment of this type of menopause is that of ovarian hormone substitution. Attempts to stimulate the ovary are very rarely successful. In the normal menopause primordial follicles vanish and ovarian atrophy takes place. F.S.H. appears in the urine and estrin, except for small quantities, vanishes. In this type of menopause estrin is of great value and in most, though not all instances, relief of symptoms is certain. The very great majority of women, however, are not troubled by the cessation of ovarian function and treatment is never sought. Only severe cases seek medical help.

The menopause as brought about by radium is caused by injury of the ovarian follicle system by the gamma rays. Primordial follicles vanish and amenorrhea occurs. Once established, this menopause is similar to that due to x-ray treatment. In the menopause due to Roentgen treatment the ovaries are injured from without inward. A failure of the follicle apparatus follows. The use of radium to bring about the menopause is probably best in that group of patients with any abnormal bleeding. In every instance a curettage for diagnosis should be done. If the menopause is sought for some other reason than abnormal bleeding Roentgen castration is just as good and probably is even more gentle. It is certain that abnormal discharges so often due to radium treatment do not accompany x-ray treated cases.

In both radiologic types of menopause recurrence of bleeding can occur. This is due to the fact that all the primordial follicles are not damaged beyond recovery and when they recover, menstruation starts again. It is not safe to assume in young women that because radium or x-ray has brought about amenorrhea menstruation will never occur again. If large doses are used it is unlikely, but the younger the patient the more the likelihood of a recurrence of bleeding. In an older patient who bleeds again after a radiation amenorrhea it is not fair to assume that the bleeding is benign. Investigation of the uterine cavity is essential to rule out the possibility of malignant disease which may have occurred during the phase of amenorrhea.

The surgical menopause is the most abrupt but the surest, and if a menopause is desired this is the most certain way to bring it about. Castration with removal of both ovaries used to be carried out much more frequently in the past decade than in this one. It is now believed that the ovaries are of great importance, so that when hysterectomy is performed before the age of 45, the ovaries are not disturbed and great care is taken not to injure the ovarian blood supply during the operation. In older women the ovaries are of less importance, but even in those supposedly past the menopause it is occasionally noted that hot flashes commence again after their removal. The abruptness of this menopause and the knowledge of the absence of ovaries gives certain women a very definite inferiority complex that is most difficult to overcome. Removal of ovaries in young people is to be deplored and great effort should be made to conserve ovarian tissue.

#### TREATMENT

The treatment of the menopause is not difficult and is usually very satisfactory. It may be carried out by means of simple sedatives, estrin, stilbestrol, progesterone, testosterone, or x-ray of the pituitary gland.

Sedatives such as phenobarbital, pentobarbital, and bromides may be used during the day and especially at night to assure quiet rest and sleep. In mild cases this simple treatment is effective.

Treatment with estrin is, however, the best method and large doses should be given at first to assure the patient relief from her symptoms. If this relief can be definite, even though the treatment is expensive, the patient will have faith. It is best to start patients with real symptoms with injections of 50,000 I.U. or 10,000 R.U. or 1.66 mg. of estradiol benzoate twice a week. Results may not be satisfactory for one or two weeks after commencing treatment. When relief is obtained the dose may be reduced to one injection per week and then to one-half the dose once per week, and so on. Eventually 200 to 600 units by mouth once or twice a week may suffice. It is first necessary to gain the patient's confidence, and then the dosage can be cut almost at will. Naturally the less treatment the better, but the mistake is usually made of trying to start with a low dose and working up, whereas it is better to start with a high dose and work down.

Stilbestrol, a synthetic substance which acts similarly to estrin, is of great value. It has definite side effects, such as nausea, vertigo, vomiting, etc., and is not yet accepted by the American Medical Association Council on Pharmacy and Chemistry. It is therefore not now recommended. If it is finally accepted it will soon replace extracted estrin because it is cheap and very effective, both by mouth and by subcutaneous injection.

Progesterin is still too expensive to use and it is not so efficacious as estrin in the treatment of hot flashes. Occasionally it may be tried along with estrin in an attempt to produce the hormone sequence for the normal person. Estrin is used for one month and during the last two weeks of the month five injections of 5 mg. of progesterone are given every other day for seven doses. In some of the difficult cases this staggering of the two hormones is of value.

Testosterone is very effective as it is a definite inhibitor of the anterior pituitary gland and therefore depresses the secretion of F.S.H. If, as we think, F.S.H. is responsible for menopause symptoms, then inhibition by testosterone ought to be useful. It is not wise to use this hormone when others are available because of its tendency to produce masculinization. It is likely that large doses would have to be given to grow hair but it would be tragic to do this if it were not necessary. If all other methods fail it is proper to give 25 to 50 mg. per week intramuscularly for a short period of time.

X-ray of the pituitary gland is not advocated, though it undoubtedly works in some cases, since it may be dangerous. If it is necessary to check the secretion of F.S.H. to stop menopause symptoms it is quite likely that some other hormone or

hormones in the gland may be depressed. Roentgen treatment of the pituitary is not recommended.

#### CONCLUSIONS

The menopause may be natural, or brought about by radium, Roentgen treatment, or surgery.

It is in most instances a natural phenomenon and is not attended by any real difficulties. It does cause severe symptoms in a certain percentage of women.

An increase of F.S.H. and a decrease in estrin in the urine is usually found.

There are many definite accompanying pathologic changes in the genital tract and probably balancing changes in most glands of internal secretion.

Treatment in most cases is very satisfactory and easy.





# THE ROLE OF ENDOMETRIAL BIOPSY IN DIAGNOSIS

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OF critical importance to the health and efficiency of the female is the ability of the ovary to discharge its two fundamental functions, ovulation and hormone production. Thus it is that we seek diligently, and prize highly, any dependable signs of ovarian activity. At present those most easily observed are found in the endometrium.

In 1908 Hitschman and Adler<sup>1</sup> described the orderly progress of the endometrium from early postmenstrual proliferation to secretion or functioning, a process which terminates with the following menstruation if conception does not intervene. In 1913 Schroeder<sup>2</sup> suggested, and quoted Meyer as agreeing, that there was a fairly accurate time relationship between these endometrial changes and the already well known ovarian sequence, that is, the progress of the ovarian follicles from early growth through maturation, ovulation, and corpus luteum formation. Causal relationship between ovarian and endometrial changes, which Knauer<sup>3</sup> and also Halban<sup>4</sup> had postulated as early as 1900, however, had not been proved.

The female sex hormone, estrogen, was shown by Allen, Doisy and Pratt<sup>5,6</sup> in 1923 to come primarily from the follicles, and in 1925 also from the corpus luteum. In 1929, Corner and Willard Allen<sup>7</sup> isolated progesterin from the corpus luteum which, in the non-pregnant, is yet its only physiologic source. It remained necessary only to prove that estrogen caused proliferation, and progesterin, secretion in order to identify the follicles and the subsequent corpus luteum as the masters of the time-related cytologic changes in the endometrium. This was demonstrated in the rabbit by Corner<sup>8</sup> and Willard Allen<sup>9</sup> in 1928 and 1930, and in the macaque by Hisaw and Leonard<sup>10</sup>

in 1930. During the next three years, Clauberg,<sup>11</sup> Kaufman<sup>12</sup> and Werner and Collier<sup>13</sup> showed that in the human, too, estrogen stimulated endometrial "proliferation" and presented adequate evidence that progesterin evoked "secretion" or "functioning." Thus "proliferation" of the endometrium indicates that follicles, the source of the estrogen which stimulates the growth, are present in the ovary, and that "secretion" or "functioning" manifests the presence of active luteal tissue. As has been prettily said by Edward Allen, we find "inscribed on the endometrium" the record of ovarian behavior.

Unfortunately, not all the endometrium records uniformly and in a critical way, the ovarian performance. To be sure, estrogen causes all areas and layers to proliferate, but only in the superficial half do the growth changes vary significantly with the orderly development of follicles from the time they escape the inhibition of the corpus luteum phase up to the maturation of one of them. Furthermore, the specific qualities of early growth and of late growth are dependably presented only in the endometrium which lines the deeper portion of the fundus.

The same localization of typically characteristic secretory changes due to the added action of progesterin on the endometrium is also recognized. Only in the superficial layers under the surface epithelium and in the adjacent glandular portion of the so-called spongy layer, and in these layers, only in the endometrium which lines the deeper half of the uterine cavity, does one find convincing evidence of combined estrogen and progesterin activity.

Biopsy of these upper reaches of the endometrial field is easy and clearly reveals the inscription of the follicles and of the

corpus luteum. The method is simple. The uterine canal is first sounded to determine its direction and the nature of the internal

luteum will be found in the descriptions which follow.

*Hypoplasia.* When biopsy obtains only

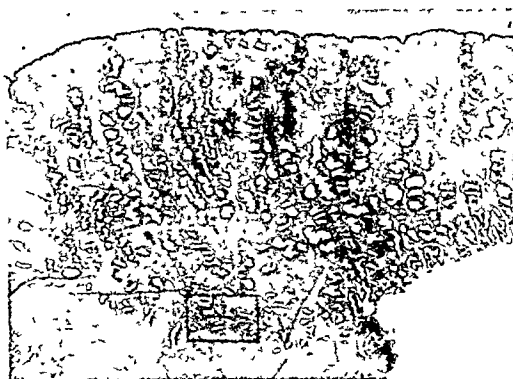


FIG. 1. Whole thickness, late secretory fundal endometrium ( $\times 17$ ). No function of basal portion. See Figure 2 for further magnification of inset. See Figure 3 for magnification of superficial late secretory endometrium.



FIG. 2. Basal late secretory ( $\times 125$ ). Dense stroma; small chromophilic nuclei; comparatively simple glands; columnar epithelium with pseudostratification in gland epithelium. No secretion. (See Fig. 3.)

os. A properly curved hollow cannula, not more than 3 mm. in diameter, equipped at the curved end with a sharp hood, or one with saw-toothed sides, and at the other end with a petcock, is then placed against the anterior wall high in the fundus. Suction is applied by a syringe attached to the outer end of the cannula while the hood is drawn firmly outward against the endometrium for a distance of about 1 cm. The cannula may be rotated and a similar stroke made against the posterior wall. The small petcock is then turned to close the cannula against a subsequent inrush of air as the syringe is disconnected. The cannula is withdrawn gently, and in such a way as to avoid clipping the internal os on the way out. The syringe is partially filled with fixing solution and reattached to the cannula; the petcock is opened; and the contents of the cannula are washed into a suitable bottle for fixing. Our custom has been to use a 10 per cent solution of formalin and to imbed in celloidin. Sections are cut as thin as possible, usually 14 microns thick, and stained with hematoxylin and eosin.

The criteria by which we believe one may deduce the presence of actively growing follicles, and of an active corpus

fragments of nondescript, fragile stroma and a few small glands, which on sectioning are frequently separated from surrounding stroma, or when the curette brings forth



FIG. 3. Late secretory from fundal portion ( $\times 125$ ). Pale stroma nuclei; distorted glands; vacuolated fragmented epithelium with basal nuclei.

only a long ribbon of surface epithelium with but meager bits of subjacent stroma attached, one may be sure that the production of estrogen is low, as in marked hypoplasia of the follicles with no approach to ovulation. It is a common finding in long-standing amenorrhea.

*Early Proliferation.* This is characterized by many straight glands of similar and constant caliber, usually sectioned in the

the most—a condition to be found only after the orderly denudation of the decidual layers. Such uniform shedding is character-



FIG. 4. Late secretory from near cervix ( $\times 125$ ). Small chromophilic nuclei. Pseudostratified columnar gland epithelium. No secretion.

same axis. These are lined by low cuboidal epithelium in which the ratio of nuclear to cytoplasmic mass is .5 or about 1 to 1. Active cell division is evidenced by a frequency of perhaps four mitotic figures in many glands. The supporting stroma is of closely packed chromophilic and practically nude nuclei.

Among these cells are many small lymphocytes, usually discrete, occasionally occurring in spheroid clumps which have been likened to lymph follicles. (These are more commonly found in more advanced proliferation.)

Though the biopsy curette removes a strip 2 to 3 mm. in thickness, there is an absence in the stroma of large irregular cavities lined by superficial epithelium so as remotely to resemble angular proliferating glands. Such units are sections of depressions in the rugous mucosa of more extensive proliferation, and their absence indicates that the endometrium is fairly smooth.

This is the cell picture drawn by the many young but actively growing follicles in a well functioning ovary during about the first six or eight days of the menstrual cycle. The similarity and simplicity of the glands, as well as the absence of sectioned endometrial valleys means that the whole tissue is but a few days old, perhaps six at

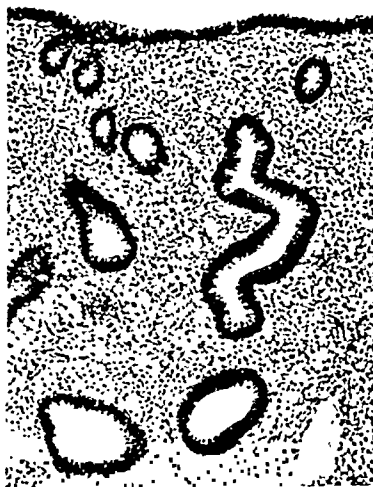


FIG. 5. Proliferative ( $\times 125$ ). Dense stroma. Pseudostratified gland epithelium.

istic only of true menstruation in a previously functioning endometrium, and so bespeaks the presence of a corpus luteum in which organization is well established, a corpus luteum whose activity was associated with atresia of the older follicles in the ovary, and whose regression saw the growth of the new crop. True postovulatory menstruation occurs not as a synchronous process in all parts of the decidua, but rather in a constantly increasing number of small foci which thus gradually include the whole surface endometrium. So, if the biopsy is made while external bleeding persists, the cytology of early proliferation may be found in one focus, while section of another area may depict menstruation.

*Late Proliferation.* This is the diagnosis when the specimen contains many sturdy, well developed glands, still of similar and fairly constant caliber, but usually sectioned in different axes, which signifies that they are slightly wavy or twisted. The gland wall is of high columnar cells in which the mass of the nucleus is to that of the cytoplasm as 1 to 2 or 3. Most characteristic is pseudostratification, i.e., the nuclei of the cells are placed at various

levels between the inner and outer borders of the epithelium. Mitotic figures occur in the luminal portion with a frequency of one or two in each of several cross sections of glands, for growth may persist until "secretion" is well established. The increase in thickness of the endometrium is accompanied by a wrinkling of its surface which permits the curette to transect it at different levels. In some places, then, the section may show only the border of a furrow between adjacent mounds. Such a depression will present in section the strangely angular lumen of what resembles a large gland lined by what might be considered atypical pseudostratified epithelium, but which is not to be confused with the lining of a gland. Such epithelium is in fact part of the surface or boundary epithelium of the mucosa. This tissue, in the human, has not yet been shown to undergo mutations characteristic of stages in the cyclical development of the endometrium.

The stroma, like that of early proliferation, is fairly dense and the cells are practically filled by the small strongly basophilic nuclei. Here and there may be seen edema, and there is almost always an occasional area containing extravasated erythrocytes. Individual lymphocytes are plentiful and so-called lymph follicles are sometimes seen. Their significance is unknown. The blood vessels are inconspicuous.

The biopsy of "late proliferation" denotes the presence in one ovary at least, of many follicles of varying ages and degrees of development, from small young follicles only 1 or 2 mm. in diameter up to several fairly large ones of a diameter of 6 to 8 mm. Such an epithelium in full flower is also found normally until several hours, doubtless twenty-four or more, after the follicle has ruptured, and so may persist for one or two, perhaps even three, days after luteinization of the theca interna has begun. If this is the case, a biopsy one week later will show the endometrium to be in the mid-secretory phase, as described below.

If menstruation occurs within ten days of the biopsy of a proliferating endometrium, one may assume it to be of the anovulatory variety, sometimes called dysfunctional uterine bleeding, for if the luteinization which evokes secretory changes is normal, it is associated soon after its inception with ovulation. Theca luteinization then normally persists and inhibits bleeding for about fifteen days from its beginning. If menstruation occurs later than the tenth day after the biopsy of a proliferating endometrium, one may only say that at the time of the biopsy there were in the ovaries some fairly mature follicles, one of which may have ruptured. If biopsies, repeated at perhaps weekly intervals, all reveal proliferating endometrium, one may say that ovulation is absent, and that the ovaries give rise to a succession of follicles which function for a time and then regress without rupture, though a few may persist as tiny cysts with little or no hormone significance.

*Hyperplasia.* This is an overgrown form of proliferating endometrium with essentially the same cytologic characteristics. The stroma may be exceedingly dense, the glands very numerous, and some of them may be markedly dilated—the "swiss cheese" endometrium of Novak.

The dilated glands are distinguished from sections of the mucosal "depression" described above, by their spherical shape, and their somewhat flattened epithelium. Such hyperplasia is found when follicles continuously develop and then either regress or persist, but fail to mature with luteinization, and so to rupture. Their prolonged secretion of estrogen stimulates the overgrowth of the tissue. Intermittent bleeding may occur from such an endometrium and so nearly in cycles as to be called anovulatory menstruation. On the other hand, it may be so irregular and so variable in amount as to merit only the term "immeasurable menstruation" or "aperiodomenorrhea." The condition is still referred to as "metropathia hemorrhagica," though it is truly an ovarian and

not a metrial dystrophy. It is also called "dysfunctional uterine hemorrhage," or "uterine insufficiency."

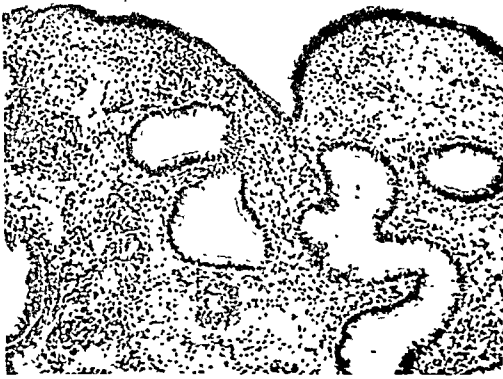


FIG. 6. Beginning midsecretory ( $\times 125$ ). Diminishing edema of stroma. Beginning enlargement of stroma cells. Dilated tortuous glands; basal nuclei; supranuclear vacuolization; beginning fragmentation of cytoplasm.

**Secretory Phase.** Secretion or function of the endometrium is characterized by five easily identified tissue mutations: (1) *mobilization outward, then inward, of the nuclei in the epithelium of the glands*; (2) *vacuolization of this epithelium with subsequent disgorgement of the vacuoles into the lumina of the glands*; (3) *dilatation, crumpling and distortion of the glands*; (4) *stromal edema, followed by enlargement of individual stroma cells*; (5) *elaboration of the vascular tree*.

We repeat: these changes occur in some degree, throughout almost all layers of the endometrium above the basal layer, but only in the superficial portion are they consistently well marked, and only in the deeper half or two-thirds of the fundal cavity do they reach their fullest expression.

Each of the five modifications mentioned as characteristic of function develops gradually, but they overlap each other and do not appear in regimented succession. The whole process of function, however, may easily be defined in three phrases: early secretory, mid-secretory (Fig. 6), and late secretory. (Fig. 3.) The sign of the first is mobilization of the nuclei, and extends about forty-eight hours after ovulation through the next three or four days, i.e., up to about the sixth day after ovulation. The

cardinal signs of the mid-secretory phase are edema of the stroma and the location of the nuclei in the base of the disgorging vacuolated cells of the gland epithelium. These two conditions appear about the sixth day after ovulation and last roughly for about four days.

The signs of the late secretory phase are enlargement of the stroma cells and increased prominence of the vascular structures. This is the period which has been characterized as showing "secretory exhaustion" (Hisaw)<sup>14</sup> and extends during the four days from about the tenth day after ovulation until menstruation.

The first change from proliferation is dislodgment of the nuclei from the bases of the cells in the gland epithelium, by chromophobic material which gives a basal lucid zone in sections stained with hematoxylin and eosin, and which reveals the presence of glycogen when stained with Best's carmine. This phenomenon in mild degree, is not specifically a progestin effect, for occasionally it is seen after prolonged administration of only estrogen in the castrate. It is rarely seen, too, in intact females from whom biopsies of persisting proliferating endometrium are obtained. In these women, however, it never reaches the stage of a prominently displayed lucid zone below uniformly mobilized nuclei; rather, it consists only of easily discerned vacuoles underlying the nuclei in some of the glands. As such a picture is also presented in the first stages of true progestin effect, it may cause some confusion in diagnosis. When due only to estrogen, it is commonly accompanied by other signs of disturbed hormonal reaction in the endometrium: more than normal are the variations in the quality of the glandular epithelium, in the size of the glands and in the density of the stroma.

More detailed description of the five prominent characteristics of function follows:

1. *Mobilization of the nuclei* by progestin moves them from placement at any level, as is seen during proliferation. First moving

them away from the base, it then groups them in the middle zone, and then, as they assume a common level, they are replaced in the bottoms of all cells, where they lie side by side. This change seems to transpire in not more than four days, approximately from the second to the sixth day following ovulation.

2. *Vacuolization of the gland epithelium* starts with the first mobilization of the nuclei, when the infranuclear vacuoles appear to dislodge all nuclei from the depths of the cells. As the nuclei accumulate in the midzone of contiguous cells the subjacent clear area becomes as large as, or larger than, the nuclei themselves. Apparently the material therein migrates centrally as the nuclei settle back to the bottom, for numerous large thin walled vacuoles appear in the cytoplasm superficial to the nuclei when these become uniformly basal. When vacuoles appear thus, throughout the supranuclear cytoplasm, the luminal border of the cell becomes frayed by their rupture. Their disgorgement continues with increasing mutilation of the cell wall and depletion of the cytoplasmic mass until finally what began as high cylindrical cells become pseudocuboidal. This process of preliminary mobilization of nuclei and subsequent depletion of the cells takes place from about the second to the fourteenth days after ovulation.

3. *Dilatation of thoroughly proliferated glands* is seen when the central surface of the epithelium becomes frayed by the evacuation of vacuoles about the sixth postovulatory day. One or two days before this the swelling of the individual epithelial cells causes a *crumpling of the glands* which forces them to assume a wavy or twisted course through the stroma, and each gland to be possibly sectioned in several different planes. As dilatation progresses, this crumpling becomes more marked and the glands become more tortuous, so that by the tenth postovulatory day, a cross section of tissue reveals lumina of various shapes and sizes, bounded by vacuolated epithelium lying in

folds or in a so-called "saw-toothed" layer. Such is the picture during the week preceding catamenia, when an organizing corpus luteum is present in an ovary.

4. *Edema of the stroma*, though appearing in slight degree in small disjointed areas of the endometrium during proliferation, becomes uniform throughout the functional layers, and extreme in amount, during the twenty-four to forty-eight hours of about the sixth to the eighth days following ovulation, after which time it gradually diminishes. The stroma nuclei are then seen connected to one another by only thin strands of cytoplasm over spaces of perhaps five to ten times their diameter. As the edema increases, the stroma nuclei enlarge and become somewhat less chromophilic. Most striking, however, after the peak of the edema and while it subsides, is the accumulation of cytoplasm in the cells, first in the vicinity of the arterioles, then alongside the glands, and just under the superficial epithelium, and finally throughout the tissue above the lower half of the spongy layer. These large, pale staining, finally contiguous stroma cells form what has been termed the *predeciduum*. The transformation occurs during the five days preceding menstruation, or from about the ninth to the fourteenth days after ovulation.

5. *Elaboration of the vascular tree* consists of a marked growth of each spiral arteriole, and an increase in the number of its terminal capillaries. When edema is extensive, the arterioles become prominent. As the edema subsides their walls are seen to be thicker, and as the adjacent stroma cells increase in size, the arteriole is found to be sectioned in more places, an evidence of increased tortuosity. The capillaries too are seen as a freely branching network in the area just under the superficial epithelium. This proliferation of the vascular system which may have begun earlier, but was obscured until edema dissected the tissue, becomes noticeable about five days before menstruation, or when the ovum is about nine days old. During the succeeding

days, individual arterioles when sectioned appear in groups of very thick walled transected loops or short segments.



FIG. 7. Postovulatory menstruation ( $\times 125$ ). Disruption of tissue; depleted gland epithelium with basal nuclei.

stromal base, may be broken to allow red blood to stream outward. When we see marked leucocytic infiltration of decidual

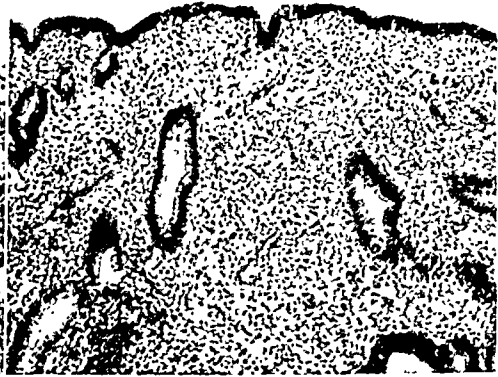


FIG. 8. Anovulatory menstruation ( $\times 125$ ). Disruption of tissue with necrosis of cells; glandular epithelium is high columnar and pseudostratified.

*Postovulatory Menstruation.* In biopsy material the process which will end in disintegration of the mucosa is seen to begin from twenty-four to forty-eight hours before disruption of the binding epithelium releases red blood into the fundal cavity. The actual process starts in isolated foci as an infiltration of the solid decidua-like superficial layer by an increased number of lymphocytes and polymorphonuclear leucocytes. The former are seen as discrete cells sprinkled freely in the tissue; the latter in smaller numbers are seen in migratory form as they are caught squeezing between the large contiguous stroma cells. The spiral arterioles are prominent but neither consistently filled nor empty, for they may be either. The capillaries, too, are sometime seen engorged with erythrocytes, in other sections, collapsed. When menstruation is but twelve to twenty-four hours distant, we find, in addition to the white cell infiltration, masses of erythrocytes free in the predeciduum, just under the superficial epithelium which is occasionally seen to be already separated from its attachment to the stroma, though still intact. When menstruation is imminent or already recently established, this extravasated blood is distributed freely in small clumps throughout the tissue, and in some places the superficial epithelium, lifted from its

like tissue, containing large irregular glands with vacuolated or cuboidal epithelium, we may be sure that progestin has been active for many days, and that catamenia is at hand. A follicle with partially organized coagulum, and a thick layer of lutein cells is uniformly found in the ovary in such a case; all of which bespeaks ovulation about fourteen days before.

*Anovulatory Menstruation.* Biopsy may reveal hemogenic disruption of a stroma which consists of the small chromophilic comparatively nude nuclei, and which surrounds the comparatively straight or gently waving glands with pseudostratified epithelium which are characteristic of a proliferative endometrium. This means shedding of a mucosa which has been subjected only to estrogen. In such cases, though menstruation is beginning, we say ovulation has not occurred, only because there has been present no corpus luteum to supply progestin sufficient to evoke the missing functional changes described above. Frequently in proliferated endometrium we see a generous infiltration of lymphocytes. This is not prognostic of flow as is the case when the completely developed predeciduum is freely invaded. At present there is no recognized cytologic sign of impending flow from a proliferative

endometrium, except gross extravasation of erythrocytes with disintegration of the stroma. Following such a biopsy there is always staining at least, and usually flow. Whether this flow would have occurred without the preceding biopsy one cannot say. Because the same quality of atypical flow occurs frequently a long time after biopsy, we may assume that the bleeding is often hormonologic and not traumatic.

*Endometritis.* When polymorphonuclear leucocytes are seen in appreciable numbers in the stroma, and, massed with lymphocytes or perhaps plasma cells and debris, in the lumina of the glands, inflammation is present. In menstruating women such inflammation is almost always chronic. Such a diagnosis should not be made when only the rather profuse but physiologic infiltration of lymphocytes is seen in proliferative tissue; nor must the similarly physiologic invasion of the late secretory and sometimes the late proliferating endometrium by lymphocytes and polymorphonuclear leucocytes be interpreted as inflammatory. Such mobilization of neutrophils precedes the diapedesis of the erythrocytes which will eventually dissolve the tissue into fragments and precipitate menstruation.

#### DISCUSSION

How accurately do the cytologic qualities of the endometrium reflect the condition of the ovarian follicular system? The author believes they do so to a high degree of probability only, which may also be said of most diagnostic procedures. Greater accuracy waits on more extensive and numerous correlated observations, but especially on further insight into the physiology of the two tissues themselves, the endometrium and the follicles. Of the former, we know little beyond its anatomy and that progressive changes therein are brought about by estrogen and progestin, acting on the glandular epithelium, the stroma and the vascular system. Of the follicles too, we know only little more than their anatomic, and to a slight degree, their hormonologic

qualities. We credit them with the production of estrogen, and to the matured form of usually only one of them each month, the corpus luteum, we attribute the production of the two hormones, estrogen and progestin. As these hormones evoke the endometrial mutations described above, so vice versa, these mutations reflect the growth of the follicles.

For the correct diagnosis of deviation from normal menstrual behavior, biopsy is of great service, and will be of increased value to the clinician when substances are isolated which will affect the germinal epithelium, either directly or through the anterior hypophysis. By reference to the endometrial condition we may learn whether immature or persisting follicles, secreting estrogen, are present or not. We may also tell whether luteal tissue is functioning; and, within the fairly narrow limits of plus or minus two days, just how long the endometrium has been subjected to the joint action of estrogen and progestin. Study already seems to show that, normally, secreting luteinized cells are active for about sixteen days. We believe too, that shortly, perhaps twenty-four to forty-eight hours after luteinization begins, the follicle normally ruptures and releases the ovum. The period from this time to normal menstruation seems fixed at about fourteen days with a remarkable definiteness, and during these days the endometrium changes progressively.

In the absence of pregnancy, the endometrium may confidently be expected to deciduate on about the fourteenth day after ovulation. Exceedingly rare cases of regression of a progestinized endometrium without flow, such as is the rule in subprimate mammals, have been observed, but as far as the author knows, not formally reported. He has himself seen one case among more than 1000, and has heard of two more. They are not to be expected. The absence of flow between a biopsy showing secretion and a subsequent one showing proliferation would discover such atavism.



By biopsy then, we may tell whether ovulation occurs and tell approximately how many days have elapsed since ovulation, and in how many more days normal menstruation should begin. If breakdown of the endometrium occurs much before the estimated date, we may safely infer a disturbance in hormonal balance which may have profound implication with fertility, for it signifies either a fault in corpus luteum physiology or in the little understood menstrual urge.

This distinction will become very important as pharmaceutical hormone preparations, which will affect either, become available. Already progesterone in repeated doses of 5 to 10 mg. may delay the destruction of the predeciduum, and estrogen in fairly large daily doses of 2000 or 3000 units may inhibit ovulation and corpus luteum formation. In smaller doses, of 1000 units or less, estrogen may be expected to stimulate corpus luteum formation and activity, probably by way of the anterior pituitary, or directly to support a functioning corpus luteum as has been shown in the hypophysectomized rabbit (Robson<sup>18</sup>). Rationally to plan hormone treatment of the female reproductive system and to estimate its effectiveness, biopsy of the endometrium is of great aid.

For correct interpretation of biopsy evidence it is usually necessary to make the examination with careful reference to periods of uterine bleeding, and especially to that flow which succeeds the biopsy. It is sometimes profitable to repeat biopsy at weekly intervals. Especially in the examination of patients complaining of infertility, and in others as well, caution must be exercised that abortion be not unconsciously perpetrated. In sterility work some prefer to perform the biopsy only during the first few hours after the beginning of menstruation. Gratifying has been the unusual induction of pregnancy apparently by biopsy performed during the post-ovulatory phase. This the author has seen in four cases. All had been inexplicably and involuntarily barren for at least two years.

They all skipped the period which was expected within a week of the biopsy. The fertilized ovum must have been present in all of them when the biopsy was made. Explanation is necessarily limited to theory.

The discovery in our clinic of four cases of unsuspected tuberculous endometritis contributes to the advisability of frequent, if not routine, biopsy examination of the endometrium.

#### SUMMARY

Since the cytologic pattern of the endometrium is specifically affected by the follicular hormones, examination of the endometrium will discover the condition of the follicular system in so far as it has hormonological activity.

The effect of estrogen and progestin is most characteristic in the superficial layers of the endometrium and in that portion of the mucosa which lines the deeper half of the fundal cavity.

Biopsy is made with an appropriate cannula by scratch with suction.

The criteria for identification of estrogen and progestin effects are given in detail. The signs of their single or joint quantitative effect, and to some extent of its duration, are expressed in the common diagnoses, hypoplasia, hyperplasia, proliferation, secretion, true menstruation and anovulatory menstruation.

Biopsy is shown to be of great assistance in the diagnosis of menstrual disturbances, in the recognition of ovulation, and for the rational use of pharmaceutical hormones and for the evaluation of their effect. It is, incidentally, of help in the detection of unsuspected tuberculous endometritis.

#### REFERENCES

1. HITSCHMAN, F., and ADLER, L. Der Bau der Uterusschleimhaut des geschlechtsreifen Weibes mit besonderer Berücksichtigung der Menstruation. *Monatschr. f. Geburtsh. u. Gynäk.*, 27: 1, 1908.
2. SCHROEDER, R. Der normale menstruell Zyklus der Uterusschleimhaut. Berlin, 1913. August Hirschwald.
3. KNAUER, E. Die Ovarientransplantation. *Arch. f. Gynäk.*, 60: 322, 1900.

4. HALBAN, J. Über den Einfluss der Ovarien auf die Entwicklung der Genitales. *Monatschr. f. Geburtsb. u. Gynäk.*, 12: 496, 1900.
5. ALLEN, E., and DOISY, E. A. An ovarian hormone: preliminary report on its localization, extraction and partial purification, and action in test animals. *J. A. M. A.*, 81: 819, 1923.
6. ALLEN, E., PRATT, J. P., and DOISY, E. A. Ovarian follicular hormone: its distribution in human genital tissues. *J. A. M. A.*, 85: 399, 1925.
7. CORNER, G. W., and ALLEN, W. M. Physiology of the corpus luteum. II. Production of a special uterine reaction (progestational proliferation) by extracts of the corpus luteum. *Am. J. Physiol.*, 88: 326, 1929.
8. CORNER, G. W. Physiology of the corpus luteum. I. Effect of very early ablation of the corpus luteum upon embryos and uterus. *Am. J. Physiol.*, 86: 74, 1928.
9. ALLEN, W. M. Physiology of the corpus luteum. VI. Production of progestational proliferation of the endometrium of the immature rabbit by progestin (an extract of the corpus luteum) after preliminary treatment with oestrin. *Am. J. Physiol.*, 92: 612, 1930.
10. HISAW, F. L., and LEONARD, S. L. Relation of the follicular and corpus luteum hormones in the production of progestational proliferation of the rabbit's uterus. *Am. J. Physiol.*, 92: 574, 1930.
11. CLAUBERG, C. Die Wirksamkeit des Luteohormons, des spezifischen Hormons des Corpus luteum, am menschlichen Uterus. *Zentralbl. f. Gynäk.*, 56: 2460, 1932.
12. KAUFMAN, C. Umwandlung der Uterusschleimhaut einer kastrierten Frau aus dem atrophischen Stadium in das der sekretorischen Funktion durch Ovariellhormone. *Zentralbl. f. Gynäk.*, 56: 2058, 1932.
13. WERNER, A. A., and COLLIER, W. D. Effect of theelin injections on the castrated woman. *J. A. M. A.*, 100: 633, 1933.
14. HISAW, F. L. Physiology of menstruation in macacus rhesus monkeys. 1. Influence of the follicular and corpus luteum hormones. 2. Effects of anterior pituitary extracts. *Am. J. Obst. & Gynec.*, 29: 638, 1935.
15. ROBSON, J. M. Maintenance and prolongation of pregnancy in hypophysectomized rabbits by oestrogenic substances. *Proc. Physiol. Soc., J. Physiol.*, 92, 1938.



# NEWER ASPECTS OF DIAGNOSIS IN EARLY CARCINOMA OF THE CERVIX UTERI

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AS the title indicates, this discussion will be limited to methods for recognizing early cancer of the cervix uteri. This also necessitates a consideration of some borderline lesions that are not frankly cancer. These areas of non-invasive carcinomatoid change are still generally recognized by the rather misleading and often misinterpreted term, precancerous, and are regarded unequivocally by some as forerunners of bonafide cancer.

We have all had the too frequent experience of observing patients who have a history of some type of bloody or malodorous vaginal discharge that has existed for months and who possess an obvious, advanced cancer when they first consult their physician. These individuals generally do not represent diagnostic problems and here the physician's responsibility in making an early diagnosis is minimal, for frequently such patients delay seeking advice not solely because of ignorance but from fear. However, even in such apparently obvious and advanced processes, it should be axiomatic that a diagnosis of cancer is never acceptable without verification by removal of tissue for biopsy.

It is true that advanced cancer of the vaginal portion of the cervix (portio vaginalis cervicis) appears as an ulcerating, friable and generally firm process of varying size, and as a general proposition it can be recognized by its gross appearance. Therefore, before one is expected to recognize cancer in its early stage, one may reasonably inquire what there is about such an obvious and well developed cancer that grossly characterizes it. The answer, heretical as it may sound, is that advanced cancer probably possesses no distinctive or grossly pathognostic appearance. Its clinical

recognition rests on the mere coincidence that most ulcerating, indurated tumors of the portio are cancer. However, occasionally such a lesion may prove to be the evidence of syphilis, tuberculosis or more rarely venereal granuloma. The reason for histologic confirmation of the clinical diagnosis is therefore obvious.

Early cancer of the cervix, merely for the purpose of clarifying the discussion, may be considered under two categories: (1) that phase where the cancer, while still small, is clinically recognizable; (2) an earlier phase in which one is not ordinarily prepared to recognize it and the gross physical aspect of the tumor is not so apparent. For descriptive purposes the latter may be considered as hidden, covert or, possibly, clinically latent cancer.

Clinically recognizable early cancer of the vaginal portion of the cervix, as physicians have been taught to recognize it, usually presents itself as a red, firm, irregular, somewhat elevated circumscribed process, situated ordinarily in the neighborhood of the external os. It generally bleeds readily on light manipulation with a soft cotton pledget and on palpation may feel indurated, although induration as a highly diagnostic sign has probably been over-emphasized. It is a lesion that should at once arouse one's suspicion as to its malignant character.

The primary prerequisites for its recognition are: adequate exposure of the cervix; adequate illumination; and deliberate, thoughtful inspection. The value of the colposcope in studying such a lesion will be discussed later. There is little doubt that, if all physicians would observe these elementary requirements, most cervical cancers would be suspected on the first examination while they were still comparatively

early and yet advanced far enough to produce slight tumefaction, a small ulcer or some other superficial change outside the normal variation, although symptoms might be entirely lacking. Obtaining tissue for histologic examination without undue delay is imperative, to establish the diagnosis and advise treatment. Especially important is it that until an adequate histologic study has been made, all attempts at treatment of such suspicious areas be withheld.

The lesion which according to my experience is most commonly suspected of being an early cancer is the vermilion zone so commonly observed about the external os. This, generally referred to as an "erosion" or "ulceration," has a well marked tendency to bleed when complicated by vaginal inflammation, which renders the red surface especially susceptible to slight trauma, with the production of minute bleeding points (erosions). Generally, however, the circumstrial vermilion zone does not bleed and does not partake of the nature of erosion or ulcer.

The differentiation of a circumstrial vermilion zone of altered epithelization from an established cancer of similar size should ordinarily not be difficult. The former may be relatively smooth and flat or it may possess a fine irregularity giving it a finely granular appearance. It does not, however, appreciably change the gross contour of the cervix. If it involves both lips of the cervix, as it often does, it has its greatest expanse on the anterior and posterior lips, with narrow lateral connecting zones of red. On palpation with a sound the surfaces are found to be elastic, and under magnification cervical glands visibly pour forth their watery secretion onto an intact, red and glistening mucosa.

A small carcinoma on the surface of the portio does not have as perfect a circumstrial distribution as the common vermilion zone does, and ordinarily it is elevated, so that it alters the contour of the cervix. Its color generally offers a distinct contrast to the surrounding mucosa, while its surface

is usually irregular and may show the opening of cervical glands. Palpation of the tumor with a sound, especially under magnification with a colposcope, reveals the irregularity previously noted and a lack of elasticity. If there is beginning degeneration of the tumor the sound can be pushed with little force into the substance of the tumor, which then bleeds readily.

A small cancer with ulceration can so simulate a benign, nonspecific, inflammatory process of the cervix, while a benign process when complicated by induration and bleeding can so mimic cancer, that their gross differentiation may be impossible. However, such instances have so far been relatively uncommon.

In summary, early cancer of the vaginal portion of the cervix that is clinically recognizable, as ordinarily encountered, presents a gross appearance which shows sufficient deviation from the normal to arouse suspicion. Obviously, its true nature may not be recognized. Nevertheless, thoughtful appraisal of the lesion on the first examination should arouse sufficient concern to stimulate the proper removal of tissue for histologic study.

#### COVERT CANCER

We come now to a consideration of those processes on the vaginal portion of the cervix which, though their appearance does not correspond to the customary gross appearance of cancer, may represent, as we have noted elsewhere,<sup>1</sup> an early phase of malignant change, i.e., covert cancer. Until comparatively recently such processes have been detected accidentally on laboratory examination and have been unrecognized clinically as either potential or bona fide early, nonulcerating cancer.

The attempt has been made to bridge the hiatus between the phase of early tumefaction and ulceration of cancer and the antecedent covert stage, in which these changes have not occurred.

Despite much effort and many reports concerning the recognition of covert cancer, instances where bona fide cancer prior

to the stage of ulceration or tumefaction was suspected clinically and verified histologically are not common. Cases reported

he must have some appreciation of the problem involved or he will find himself faced by one dilemma after another. Our

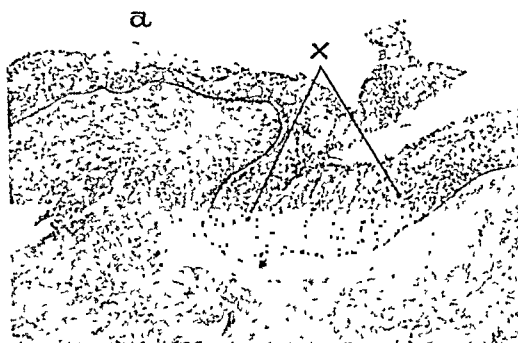


FIG. 1. Illustrates the epithelial change that may occur at the margin of a bona fide cancer. At *a* the epithelium is essentially normal while at *x* it has all the histologic characteristics of cancer but without invasion. (From Martzloff, in *Bull. Johns Hopkins Hosp.*, 33: 221, 1922.)



FIG. 2. From same specimen as Figure 1. *a*, the cervical canal; *b*, a club-shaped mass of cells histologically identical with cells at *x* in Figure 1; *c*, clumps of cancer cells in lymphatic spaces. Figures 1 and 2 illustrate the necessity of adequate tissue for histologic study if a proper differentiation is to be made between an early cancer such as this and a lesion showing only "non-invasive carcinomatoid change" as illustrated by Figure 3. (From Martzloff, in *Bull. Johns Hopkins Hosp.*, 33: 221, 1922.)

by Haselhorst<sup>2</sup> and Marti<sup>17</sup> are possibly such examples. Attention has been focused on these areas and other areas of a more controversial character by Hinselmann<sup>3</sup> and by Schiller.<sup>4,5</sup> Generally such an area on examination with a speculum appears as a white, opaque, sometimes slightly wrinkled plaque, which may appear somewhat raised, of varying size (usually small), which is termed a leucoplakia. It is believed by some that cancer of the cervix in its earliest grossly recognizable form reveals itself as a leucoplakia (white spot). The problem would be simple if this were the entire story. However, when one enters into a discussion of leucoplakias which are considered cancerous because their epithelium shows a superficial carcinomatoid change, one becomes involved in the vexatious question of how to recognize histologically that such an area is truly an incipient cancer and therefore destined to become invasive. Obviously, this is a problem with which the practicing physician does not ordinarily have to concern himself since he feels that is the pathologist's problem. However, if the practicing physician is to concern himself with the matter of detecting covert cancer and the methods proposed for accomplishing this,

discussion of this will be brief since it concerns those non-invasive carcinomatoid changes in the cervical epithelium which are recognized by such terms as precancerous, cancer in situ, probable beginning cancer, intraepithelial cancer, Bowen's disease, non-invasive potential carcinoma, etc.

In short, cancer of the vaginal portion of the cervix in its incipency is assumed to pass through a stage in which the cells of the stratified epithelium in a given area possess all the histologic earmarks of cancer but lack the property of invasion.

Laying aside all theoretic considerations, one cannot say positively whether the ultimate fate of such suspicious lesions after a varying period of latency will be one of steady progression to invasion and full-blown malignancy or whether there may occur a process of regression and restitution to normal. Similar epithelial changes are occasionally found at the periphery of bona fide cancers, and it is therefore necessary when the histologic picture of a

non-invasive carcinomatoid change is seen to make certain that the material has not come from the margin of a full-blown malignant process.

In practical application, the instances of covert cancer so far reported, with few exceptions, fall into this group showing non-invasive carcinomatoid change. Since some observers consider such areas as bona fide local cancers, therefore possessing the power of ultimate destructive invasion, it appeared logically imperative to develop some means for their detection at a time when ulceration or tumefaction were absent.

*Methods for Revealing Areas of Abnormal Epithelial Change.* Two methods to solve the problem have been proposed almost simultaneously. Both have for their ultimate aim to render visible the areas under consideration, but the procedures used to bring this about are fundamentally different.

The first is the *iodine test* proposed by Schiller to study the tinctorial reaction of the stratified epithelium of the vaginal portion of the cervix. The rationale underlying this test, which is described in the next paragraph, is based on the observation of Lahm, Schiller and others that histologic preparations of cancerous epithelium when stained for glycogen usually show it as absent. Langhans has shown that glycogen in living tissue stains with iodine. Using this observation Schiller has been able to demonstrate that the cells belonging to areas of non-invasive carcinomatoid change as well as the grossly normal, but cytologically cancerous epithelium that surrounds some well established cancers does not give the dark brown color reaction as does normal epithelium. The difference in the staining reaction between the two types of intact epithelium offers a sharp and visible contrast which the alert examiner cannot easily overlook.

The iodine test is done as follows: The cervix is exposed as in any speculum examination and excessive secretion is gently wiped away with cotton. A cotton

pledget dripping with Gram's iodine solution (iodine 1 part, potassium iodide 2 parts, water 300) is applied repeatedly to

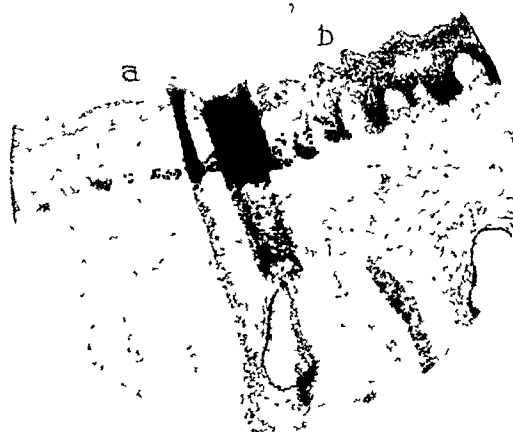


FIG. 3. From a cervical polyp. *a*, essentially normal stratified cervical epithelium, while at *b*, the epithelium has undergone a profound and abrupt change. Here the cells are irregular in size, shape and staining reaction, layer formation is lost and from three to five mitotic figures may be seen in some high power fields. This is a typical example of non-invasive carcinomatoid change (so-called superficial cancer, precancerous lesion, etc.). This area is small, circumscribed and no invasion is demonstrable. Otherwise its appearance is as typical of cancer as the cancerous areas in Figures 1 and 2. Some leucoplakiae possess a similar histologic structure. (From Martzloff, in Dean Lewis' Practice of Surgery, Prior.)

the cervix until it takes on a deep chestnut brown color. It requires several seconds for the color to develop. Pathologic epithelial areas, in particular cancer epithelium, according to Schiller, take no stain or at most assume a faint yellow color and therefore stand out in distinct relief. The iodine solution should be comparatively fresh.

The other method depends on the use of the colposcope. This was devised by Hinselmann as a result of his observation of two large areas of leucoplakia (white plaques) on the vaginal portion of the cervix. Histologically these areas showed the cellular changes ascribed to cancer (mitoses, irregularity in size, shape, relationship and staining reaction of the cells), but they were limited to the anatomic

confines of the epithelial zone, i.e., invasion was lacking. On the basis of this observation and a few earlier observations by von

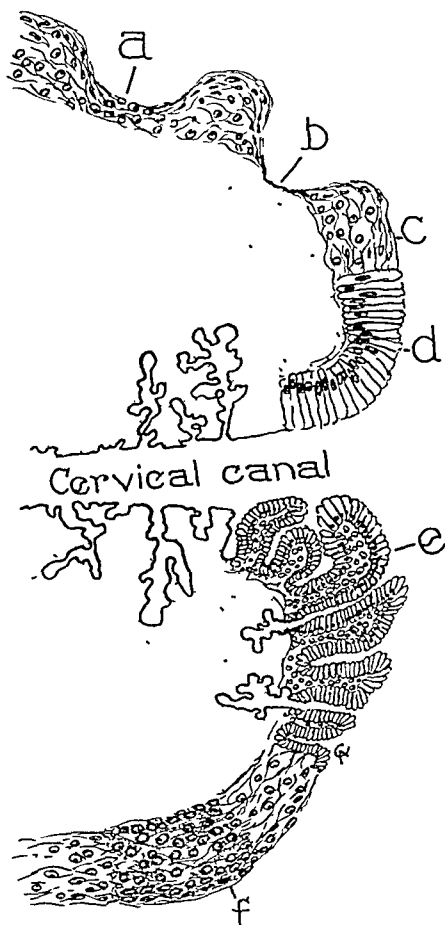


FIG. 4. Schematic representation of the portio vaginalis cervicis to show some of the types of areas that react differently to the iodine test. *a*, superficial erosion that does not stain. *b*, a deep erosion or small ulcer that may take a brown or modified brown color. *c*, normal stratified epithelium which stains mahogany brown. *d*, columnar epithelium that has grown out from the cervical canal on to the portio to produce the familiar vermillion zone about the external os which retains its red color just as does area *e* with the iodine stain. *e* is frequently and incorrectly termed a papillary erosion, but differs from *d* only in that it has a papillary structure. *f*, an area of non-invasive carcinomatoid change or a leucoplakia which does not stain. (From Martzloff, in *Internat. Clin.*, 4: 179, 1934.)

Franqué and others, which have been discussed elsewhere,<sup>6</sup> it appeared reasonable to infer that leucoplakia offered a starting

point for cancer. Indeed, it has long been held by von Franqué<sup>7</sup> that cancer of the portio probably manifests itself first as a leucoplakic change and, conversely, that certain leucoplakic plaques are destined eventually to become cancers. It therefore appeared logical to attempt to recognize these changes in their incipience when they might be so small as to escape observation by the unaided eye. The magnification from 10 to 15 diameters which the colposcope provides is designed to make such recognition possible and also to permit study of lesions other than leucoplakia.

Study of the cervix under magnification is interesting and informative if one controls one's observations with histologic studies. One learns that the cervix generally has a slight but definite pulsation synchronous with the heart beat; that cervical glands may open onto the portio 1 or 2 cm from the external os through a normal, stratified epithelium, which is bathed by their intermittent, crystal-clear secretion, and that gland openings commonly occur also in the circumstrial vermillion zone and may have there small yellowish gray plugs simulating leucoplakia. Also it is not uncommon to note at the transition zone, where the pale pink of the normal stratified epithelium meets the bright red of the thin epithelium of the vermillion zone, areas where the epithelium is pale gray, almost white. Minute bleeding points (erosions) and small ulcers can be readily identified, as can also other more major deviations from the normal.

**Results of Tests.** The question naturally arises as to how valuable these two methods are for the recognition of incipient cancer or areas of non-invasive carcinomatoid change, when compared with ordinary methods of careful inspection.

Our experience with these methods now extends over approximately nine years. Unquestionably the iodine test is not specific for cancer or for areas of so-called non-invasive carcinomatoid change. Schiller originally pointed out some of the pitfalls in this test, but felt that nonstain-

ing areas are often, though not always, cancerous. According to our experience the overwhelming majority of unstained areas, including areas of leucoplakia, shows no histologic evidence suggestive of a non-invasive carcinomatoid change. Small epithelial gland plugs, vermilion areas, a proportion of superficially situated Nabothian follicle cysts, areas of epithelial loss, either when superficial or, if complete, apparently when fibrin covers the base of the ulcer, epithelium involved in an underlying inflammatory process and particles of adherent inspissated secretion, together with other unexplained areas, fail to stain with the iodine. It follows that if areas that do not stain with iodine are not interpreted with due reserve they lead to endless confusion and alarm for the physician and unnecessary removal of tissue for biopsy, cervical tinkering and hysteria for the patient.

Up to the present time I have not discovered a histologically proved area of non-invasive carcinomatoid change with the iodine test, nor has the test, which is used routinely, so far proved to be of any more assistance than careful inspection with the unaided eye.

The altered epithelium that does not stain with iodine which occurs at the periphery of some established carcinomas has, as in Henriksen's case,<sup>8</sup> occasionally led to the suspicion and recognition of a cancer. So far, however, in most of such published instances<sup>9</sup> a history of bleeding and an ulcerating cancer were present which should have caused suspicion from the beginning. It is probably permissible to conclude that in its general application a test as unspecific as the negative iodine reaction is likely to be more confusing than helpful. Certainly, as has been noted elsewhere,<sup>10,11</sup> the test is not pathognomonic of a malignant condition, though it may possibly be a signal which calls for further study.

The colposcope, since it facilitates visual observation of the cervix uteri, would naturally appear to answer an unfulfilled

need and to fall into the category of nasal and aural specula, the proctoscope and the cystoscope. However, the comparison is

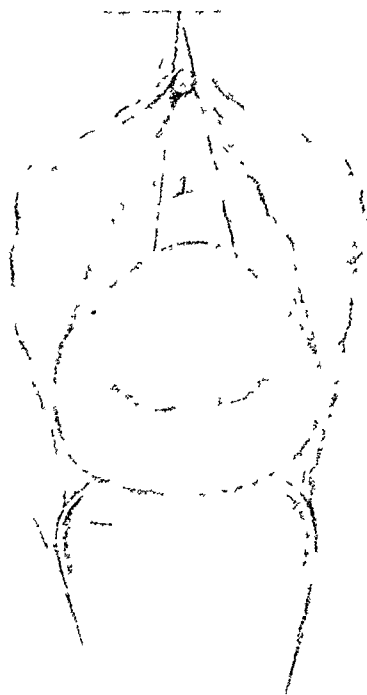


FIG. 5. A leucoplakia involving anterior cervix at external os and extending into canal. Histologic study revealed nothing noteworthy except a superficial stratum corneum.

not so apt as it sounds, for from the standpoint of the profession at large it has several drawbacks which probably will prevent its general adoption. These include the expense of the instrument, the time necessary to make a careful study and the need of extended experience to interpret correctly what one sees. The need of extended experience makes it necessary for the clinician to use the instrument regularly and to correlate the colposcopic appearance of the cervix with the histologic picture of the area in question. This requires frequent diagnostic section and study of the tissue by the clinician himself. The obtaining of tissue for biopsy takes the method out of the realm of simple non-technical procedure, for if an area is sufficiently abnormal in appearance to warrant removal of tissue, removal should be carried out as described later. An



inadequate specimen for biopsy is probably worse than none, for it frequently makes it impossible for the pathologist to arrive at a correct interpretation. If cancer is present and the specimen does not contain any of it the patient's welfare is unjustifiably jeopardized.

The colposcope, since it aids in inspection, is a fundamental contribution to methods of visual examination of the vaginal portion of the cervix uteri. While we use it as a routine, it has been of essential value in only a few instances. So far we have discovered with it neither areas of unmistakable non-invasive carcinomatoid change, non-ulcerating (covert) cancer, nor any small cancerous ulcers which could not be detected with the unaided eye on careful methodical examination. It is important to appreciate fully that the gross appearance of the small lesion of early established cancer, as pointed out by Hinselmann,<sup>12</sup> is not sufficiently characteristic to permit its differentiation from other nonmalignant lesions solely on the basis of its appearance through the colposcope.

The impression therefore is inescapable that for the present the recognition of cancer of the cervix uteri in its early stages still rests on painstaking visualization and inspection and proper obtainment from unusual appearing areas of tissue for microscopic examination. To await the appearance of a large ulcer formation, obvious induration or a cauliflower-like tumefaction such as that described in textbooks before clinically suspecting cancer is like preparing for sea after the ship has sailed.

This critical evaluation of methods more or less recently popularized for the apparent simplification and ready determination of early cervical cancer should not be construed as unfriendly criticism, for there are those who are enthusiastic concerning their value.<sup>13-16</sup> However, as noted before, on the basis of a fairly long and appreciable experience we agree with those<sup>17-19</sup> who believe that these methods possess greater limitations than are ordinarily ascribed to them.

#### ENDOCERVICAL CANCER

So far our discussion has concerned itself solely with cancer arising on the vaginal portion of the cervix. Obviously early cancer arising in and still confined to the cervical canal does not lend itself to the same methods of detection as do similar lesions on the portio. Endocervical cancer is therefore generally unsuspected and undetected until it gives rise to symptoms which are almost without exception due to a breaking down of tumor tissue. This ordinarily produces some type of bloody discharge which may or may not be malodorous. A small bit of cancer epithelium may plug the cervical canal long enough to produce a small pyometra which, when it finally expels the friable cancerous obstruction, produces a sudden, copious gush of malodorous secretion which is the first sign of mischief. Obviously inspection of the cervix when the cancer is small and well within the canal is irrelevant and the presence of a malodorous blood tinged discharge is certainly not diagnostic of cancer, although it should be so considered until it is proved otherwise. The sudden copious discharge of pent-up secretion is, of course, practically pathognostic of a cervical obstruction which may be benign or malignant.

Naturally when an occult endocervical cancer is suspected, as a matter of routine, the entire uterine cavity should be regarded with misgiving until proper study has fixed the type and site of pathologic change. The problem of diagnosing suspected endocervical cancer is considerably more difficult technically than that presented by a suspicious nonsymptomatic area on the portio which has been discovered possibly with the aid of the iodine test or the colposcope. This is because an endocervical cancer when it first produces symptoms may be early or well advanced, but it is generally complicated by infection. If a pyometra is present immediate extensive manipulation is contraindicated.

*Procedure for Routine Study to Detect Early Asymptomatic Cervical Cancer.* The

clinical methods we have described for detection of areas suspicious of early cervical cancer are applicable only to the vaginal aspect of the cervix, and in the course of such a survey an early asymptomatic endocervical cancer may be overlooked. In order to try and avoid this oversight it is advisable to employ a definite routine somewhat as follows:

1. Customary bimanual abdominovaginal and abdominovagino-rectal examination. We generally do this after the speculum examination.

2. Meticulous examination of the vagina and cervix through a speculum. For this the patient should be in the lithotomy position and adequate illumination obtained either with a head mirror or an illuminated speculum.

- (a) Colposcopic study of the cervix (optional).

- (b) Staining reaction of the cervix to Gram's iodine solution (optional).

- (c) Exploration of the endocervix.

The most distal portion of the endocervix, if the external os is large enough to permit it, is inspected by separating the lips with long tissue forceps or other suitable instrument. In this way in favorable instances the lower 1 or 2 cm. of the cervical canal may be clearly visualized.

A small sound is then passed the entire length of the cervical canal after the cervix has been cleansed and a suitable antiseptic applied. This maneuver will reveal among other things an unsuspected stricture and friable tissue, if present in sufficient amount. If bleeding follows this type of cervical exploration and no definite stricture or friable tissue is detected, 10 per cent silver nitrate may be applied to the cervical canal and the patient asked to return in five to seven days. Such bleeding generally is not due to cancer. On the subsequent visit, the canal is once more explored with a sound. If bleeding again occurs a special small, narrow, sharp curette may be gently employed to remove any tissue that comes away with light pressure. This is immediately fixed in 10

per cent formalin and used for microscopic study. Obviously a supravaginal hysterectomy should not be done closely after this type of procedure.

When bleeding occurs and one is suspicious of friable endocervical tissue at the time of the first cervical exploration with the sound, further study should not be done until proper operating room and laboratory facilities are available.

Whether the area suspected of possible malignancy lies on the vaginal portion of the cervix, within the cervical canal, or both, one is immediately confronted with the necessity of obtaining tissue for biopsy.

#### BIOPSY

Here again our discussion is concerned solely with the problem of obtaining tissue for diagnosis from suspicious areas that may harbor either *bona fide* covert cancer or areas that represent a non-invasive carcinomatoid change. The matter of obtaining tissue for biopsy under these circumstances becomes one of real importance, for unless the tissue is adequate and properly obtained, it may be impossible to have sufficient material on which to base a diagnosis. Particularly true is this when there is a question whether a given lesion represents a *bona fide* malignancy or merely a non-invasive carcinomatoid change.

No hard and fast rules can be laid down for obtaining tissue for biopsy in each variety of lesion. Only broad general principles can be indicated. Most pathologists can testify to personal experience with tissue submitted to them from cancer-afflicted patients which either showed no cancer or was of debatable character while full-blown carcinoma existed a few millimeters from the site of the specimen. Tissue removed from a small circumscribed area suggestive of cancer should include both material from the suspicious area and a generous amount of adjoining normal-appearing tissue. The block so obtained should be rectangular or nearly so, as shown in Figure 9, and should immediately

be fixed in solution of formaldehyde or other suitable fixing solution. If the material is obtained and prepared in this

procedure combined with amputation, as described by Te Linde,<sup>20</sup> is a convenient method of simultaneously obtaining mate-

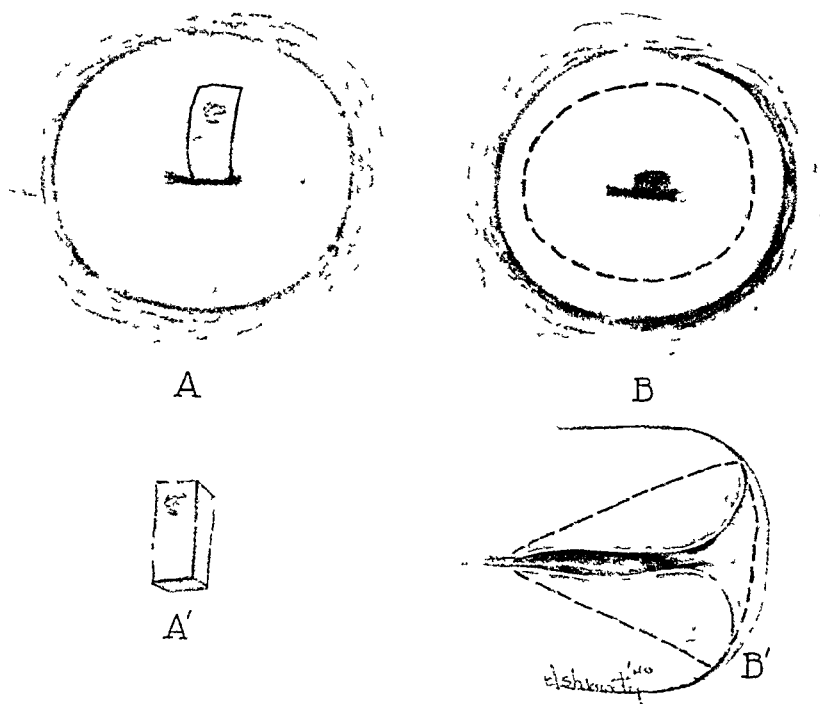


FIG. 6 Schematic representation of the method of obtaining material for histologic study. A represents a suspicious area on the anterior lip of the cervix uteri, with the dark lines indicating the direction of incisions for removal. A', the shape of the excised block of tissue. B, a larger suspicious area, which in some cases may advantageously be removed by a cone-shaped enucleation of the endocervix, together with a portion of the portio, as indicated by the circularly dotted line and also as represented by shaded area in B'.

way, when it is ready for microsectioning there is little doubt about the direction in which the block should be cut. Minute fragments of tissue, wedgeshaped pieces of tissue and material obtained by scooping out tissue with the endothermy loop may be entirely unsatisfactory. The advisability of curetting the surface of the process as has been recommended is also a dubious procedure. Ordinarily there can be little excuse for such haphazard methods when the lesion is small, circumscribed and primarily a diagnostic problem.

When the area under suspicion is more diffuse, extends into the cervical canal, or is located on a cervix that otherwise merits some form of operative correction, an amputation or preferably a Sturmdorf

procedure combined with correcting a local pathologic condition. Whether the scalpel or the endothermy current is employed for this purpose probably matters little. However, if the latter is used one should allow for destruction by heat along the margins, where the fragment of tissue becomes unsuitable for histologic study. When a tumor is large and its character obvious, naturally observance of such minutiae is not essential.

It is important if a conical enucleation of the endocervix is done, that the dissection be carried sufficiently proximally and widely so that all the mucosa is obtained. (Fig. 9B.) This is not a simple office procedure and should not be done with the small endothermy units common to

office practice, although such a procedure is advocated by some.

The importance of this cannot be overstressed in these instances where varying portions of the mucosa of the canal have undergone stratification (squamous cell metaplasia) and the glands are filled with stratified epithelium. This in the absence of any further change is occasionally erroneously diagnosed as cancer. However, when this stratified epithelium really takes on the appearance of cancer, it becomes of vast practical importance to know whether it is an invasive tumor, even though minute, or merely an area of non-invasive carcinomatoid change, and, if the latter, whether it has been entirely removed. This requires the preparation and study of numerous microsections—which cannot be done in a few minutes while the patient is on the operating table under anesthesia.

The clinician must therefore do his part by properly obtaining tissue. It then becomes the problem of the pathologist, if the clinician is not versed in gynecologic pathology, to make a histologic diagnosis. This ordinarily provides the key to the problem of the patient's subsequent management. However, where the lesion is one that presents difficulty in diagnosis, and this does happen, it is desirable that the clinician have sufficient understanding and experience to appreciate the pathologist's dilemma. Thus the patient's interests may be protected and her welfare not jeopardized by the use of therapeutic measures for which there is strong emotional impetus but a poor factual basis.

The diagnostic problems presented by these areas of non-invasive carcinomatoid change (precancerous lesions) have been well described by Novak,<sup>21</sup> Freedman,<sup>22</sup> Schiller,<sup>23</sup> Te Linde,<sup>24</sup> von Franqué,<sup>25</sup> Pemberton and Smith,<sup>26</sup> and more recently by Stevenson and Scipiades<sup>27</sup> and others. It is obvious that they offer problems toward which various students of the question assume varying points of view. With this as a basis, the therapeutic approach varies from one of careful study and simple

removal of all suspected tissue, if the original operation for the removal of tissue for biopsy has not accomplished this, to a thoroughly energetic program of radiation, radical operation or radiation and operation. In other words, we find illustrated here the conservative versus the radical therapeutic approach to a problem whose true significance is probably little better understood now than it was by Virchow<sup>28</sup> eighty years ago.

Our attitude toward these borderline lesions of non-invasive carcinomatoid change when sufficient tissue is available for adequate study has been similar to that of Te Linde, Novak, and a few others, one of conservatism. Our limited experience is borne out by the studies of others,<sup>24,27</sup> where following removal of such suspicious cancer-like lesions, nothing more was done. Especially valuable are the observations of Stevenson and Scipiades on eighteen patients so afflicted. The diagnosis of "non-invasive potential carcinoma" had been made in thirteen of these, from three to seventeen years before. The outcome is known in eleven. Only one was treated with radium and two were under observation for less than six years. Two of these eleven patients later developed cancer, one nine years after she was first seen when she had a full-blown cancer of the portio, the other three years after her biopsy when she died of pernicious anemia and the cervix removed at autopsy revealed a small bona fide cancer detectable only on histologic study. The others remained well.

It is obvious that some of these borderline lesions that are coming to our attention more frequently, now that early malignant changes are being more carefully sought, offer special problems for the clinician and the pathologist. The present status of our knowledge based on adequate study of tissue and follow-up of patients is still not sufficient to warrant a hard and fast attitude on the subject. This certainly is not conducive to a complacent state of mind. As a consequence, it has led some to adopt the attitude that granted the le-

sion of non-invasive carcinomatoid change is not definitely cancer, nevertheless, if it is treated as such there is eliminated the danger of future malignancy.

This is often regarded as a straightforward, practical, point of view which presumably leaves little room for improvement. It is, however, an attitude based largely on fear and lack of information. This not only stifles inquiry and progress, but leaves in its wake women too often in the prime of life who have become victims of well intentioned but ill conceived radical therapy. Further study of such surgically removed organs often reveals little to justify such procedure.

#### CONCLUSIONS

The conclusion is permissible that the problem of early and especially of covert cancer of the cervix uteri and the allied pathologic problem of non-invasive carcinomatoid change often require special consideration and study. It therefore follows that adequate removal of tissue from a so-called suspicious area together with a careful and competent histologic study are the foundations on which rest the diagnosis of early cancer of the cervix uteri.

#### REFERENCES

- MARTZLOFF, K. H. Cancer of the cervix uteri; recognition of early manifestations. *J. A. M. A.*, 111: 1921, 1938.
- HASELHORST, G. Portioleukoplakie und Karzinom. *Ztschr. f. Geburtsb. u. Gynäk.*, 101: 622, 1932.
- HINSELMANN, H. Die Kolposkopie in der ärztlichen Praxis. *Monatschr. f. Krebsbekämpfung*, 5: 121, 1937.
- SCHILLER, W. Zur klinischen Frühdiagnose des Portiokarzinoms. *Zentralbl. f. Gynäk.*, 52: 1886, 1928.
- SCHILLER, W. Early diagnosis of carcinoma of the cervix. *Surg., Gynec. & Obst.*, 56: 210, 1933.
- MARTZLOFF, K. H. Leukoplakia of the cervix uteri; a manifestation of early malignant change? *Am. J. Obst. & Gynec.*, 24: 57, 1932.
- VON FRANQUÉ, O. Leukoplakie und präcanceröse Veränderung des Plattenepithels. *Zentralbl. f. Gynäk.*, 51: 898, 1927.
- HENRIKSEN, E. Precancerous and carcinoid lesions of the cervix uteri with comments on the Schiller test. *Surg., Gynec. & Obst.*, 60: 635, 1935.
- GRAVES, W. P. Detection of clinically latent cancer of cervix. *Surg., Gynec. & Obst.*, 56: 317, 1933.
- MARTZLOFF, K. H. Recognition of early cancer of cervix uteri. *Internat. Clin.*, 4: 179, 1934.
- MARTZLOFF, K. H. Early cancer of the cervix uteri; practicability of its recognition before the stage of ulceration. *Northwest Med.*, 34: 295, 1935.
- HINSELMANN, H. Die klinische und mikroskopische Frühdiagnose. *Arch. f. Gynäk.*, 156: 239, 1933.
- GEISENDORF, W. Quelques notes sur la colposcopie. *Bull. Soc. gynec. et obst.*, 28: 128, 1939.
- WESPI, H., and BRASCH, D. Zur Frühdiagnose des Portiokarzinoms. *Monatschr. f. Geburtsb. u. Gynäk.*, 109: 4, 1939.
- MESTWERDT, G. Zur Frage der Diagnose des latenten Portiokarzinoms. *Zentralbl. f. Gynäk.*, 61: 2742, 1937.
- MÖNKEBERG, A. Auch ein Anfänger kann das Portiokarzinom im ersten Beginn mit dem Kolposcop entdecken. *Zentralbl. f. Gynäk.*, 62: 52, 1938.
- MARTI, T. Bieten die Schiller'sche Reaktion und die Kolposkopie eine hundertfache Sicherheit bei der Frühdiagnose eines Plattenepithelkrebses an der Portio? *Zentralbl. f. Gynäk.*, 63: 1460, 1939.
- REEB. Discussion of paper by Geisendorf.<sup>13</sup>
- WINTER, G. Das Kolposkop bei der Krebsbekämpfung. *Zentralbl. f. Gynäk.*, 61: 2147, 1937.
- TE LINDE, R. W. Amputation of the cervix with application of the Sturmdorf flap principle. *Surg., Gynec. & Obst.*, 43: 513, 1926.
- NOVAK, E. Pseudomalignant and precancerous lesions of the cervix. *J. A. M. A.*, 108: 1145, 1937.
- FREEDMAN, N. Precancer of the cervix uteri. *Surg., Gynec. & Obst.*, 58: 717, 1934.
- SCHILLER, W. Leukoplakia, leucokeratosis and carcinoma of the cervix. *Am. J. Obst. & Gynec.*, 35: 17, 1938.
- TE LINDE, R. W. Cancer-like lesions of the uterine cervix. *J. A. M. A.*, 101: 1211, 1933.
- VON FRANQUÉ, O. Anatomie, Histogenese und anatomische Diagnostik der Uteruscarcinome, Veit-Stoeckel Handbuch der Gynäkologie, vol. 6. Munich, 1930. Bergmann.
- PEMBERTON, F. A., and SMITH, G. VAN S. Early diagnosis and prevention of carcinoma of the cervix. *Am. J. Obst. & Gynec.*, 17: 165, 1929.
- STEVENSON, C. S., and SCIPIADES, E. Non-invasive potential "carcinoma" of the cervix. *Surg., Gynec. & Obst.*, 66: 822, 1938.
- VIRCHOW, R. Cellular Pathology, 8th American Ed. Philadelphia, 1859. Blakiston.



# THE PRESENT STATUS OF RADIUM TREATMENT OF CARCINOMA OF THE UTERINE CERVIX

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IT seems rather remarkable that, after more than fifty years of intensive study of cancer of the uterine cervix, the medical world knows so little about the laws that govern its origin and growth. It seems equally remarkable that so many important observations about this cancer appear to have been forgotten, probably because they were made when surgery alone offered any hope of cure and before any one was conscious of the therapeutic value of radium. The modern cancer student now usually has a background of some animal experimentation, a study of physics, and has had an intensive training in therapy with radium and with the heavy voltage Roentgen ray. Yet he rarely has had much of an apprenticeship in cancer surgery, and in all probability was taught erroneously that the radical operations for cervical cancers were only conspicuous failures attended with an operative mortality of 20 per cent. Usually he is not much interested in what happened in the surgical era.

Yet nearly all that we know of the methods of growth and extension of untreated cancer was learned during the surgical period. When men were attempting to cure extensive cancers they had remarkable opportunity to see all types of invasions. Among the many things that they learned we note the following:

Cancer may not grow at the same rate of speed in women even in the same age group and same body build.

Cancer may use different pathways for extension and finally present such great variation in its morphologic picture that one might almost conclude that they were different cancers. Ries and other early workers described a number of these, many of which now constitute the sub-

groups in the recent League of Nations classification.

The average duration of untreated cancer is about two years; the extremes are shown in Table 1. The reasons for these variations have never been determined. There was some evidence that cancer grows more rapidly in the anemic flabby body than in the compact well nourished individual, yet there are many exceptions to the rule.

TABLE 1  
DURATION OF LIFE IN UNTREATED CANCER  
Stage 4 Cancers (Schmitz)

Symptoms before Treatment	Cases	Survival after Treatment, Months
0-3 months.....	13	7
3-6 months.....	17	7½
6-9 months.....	13	9
9-12 months.....	8	7
12-18 months.....	14	12
18-2 years.....	3	8½
2 years and over.....	14	10½
Unknown.....	2	14
Total.....	84	

It was well recognized that there was great variation in the time when the glands became involved. Usually, but not always, the parametrium seemed to be first invaded. Yet enlarged firm glands have been found to be free from cancer, and enlarged only from absorption from the inflammation of cancerous ulcer. On the contrary, small normal-appearing glands have shown definite cancerous infiltration even with a soft parametrium, and in quite recent time Bonney showed that the obturator glands were invaded very early—a fact that had not been recorded by the earlier observers.

George Winter noted that patients whose cancers presented everted or papillary or cauliflower forms usually survived longer than those who came with cancers inverting and infiltrating.

Schottlaender, as early as 1906, attempted to link rapidity of growth with the histologic cell picture, giving the foundation on which Broders and Martzloff laid their work many years after.

With such a kaleidoscopic mass of facts before us, no one should be surprised to learn that a definite percentage of patients who seemed to be inoperable before operation survived the radical removal and the five year observation period without evidence of recurrence, and that some patients whose visible growth was limited clearly to the cervix, died from recurrence in a few years after a radical operation. There is no doubt but workers in the surgical era proved that there were great variations in the malignancy of what appeared as the same type of cervical cancer.

Radium when first introduced was given only to inoperable cases, but such remarkable results attended its use that many felt that they were justified in radiating early operable cancers instead of operating upon them. In spite of the fact that no one knew anything much about proper doses, foul smelling ulcers cleared up, hemorrhage was arrested, patients gained in weight and strength, and some who even looked as if they were about to die seemed tremendously improved.

The few fistulas which followed the treatments seemed nothing in comparison to those attending surgery. More than that, patients left the hospital on their own feet, and cancer wards no longer were filled with dying women surgery had failed to cure. It is no wonder that the world fairly went mad about radium. I much doubt if any other discovery in recent medicine has been as dramatic.

Time has proved that radium cannot accomplish all that was once claimed for it. It has done wonders, but probably the limits of its therapeutic possibilities have

been reached; there is no doubt whatever that the combination of deep Roentgen ray and radium accomplishes far more than either treatment used alone. No one, however, feels that even this combination therapy is the final answer to the problem of successful treatment of cancer of the uterine cervix.

The reason for this change of thought about radium has followed the observations that the element is unable to kill cancer more than a few centimeters from the point of application, unless tremendous dosage is given with the bomb. Even then there may be cancer cells that do not succumb to the rays, in the tissues which should be perfectly rayed. Unfortunately no one knows much about these radium-resistant cancer cells.

When radium first came into therapy, it was thought that a capsule placed in the cervix, which is practically the center of the pelvis, would completely ray all cells within the pelvic walls, killing all the cancer cells within the pelvis but not harming the normal tissues. There seemed much clinical evidence for such belief; not only did the local lesion shrink up and disappear but occasionally the treatment seemed to cure cancers with parametria so involved that they had to be classed as inoperable.

Few have removed such uteri to study the pathologic picture. Following our gland resection operations it has been necessary occasionally to remove the pelvic organs in such cases. In some we have not been able to demonstrate cancer cells in the parametrium, forcing the conclusion that the infiltration had been inflammatory only from absorption from the infected ulcer, which cleared up when the ulcer had been cured; this of course means that the case had not been inoperable. When unchanged cancer cells were found in the parametrium and the glands were found not involved, many questions naturally arose. For instance, one would wonder whether this cancer was of comparatively low malignancy and was invading slowly, and whether it would have lain dormant for some

time after the inflammatory products had cleared up after radiation if it had been radiated only and not operated upon. Cases like these with limited invasion must have been the bulk of inoperable cases which became five year cures after radical operation in the older days, in the surgical era.

We now know that all that we hope radium will do, when inserted into the lower uterine canal and cervix and the dose is adequate, is to take care of the cancer in the lower uterine and cervical walls. It cannot kill cancer cells even in the parametrial cervical-uterine margins; those must be taken care of by cross-firing from the vagina, by parametrial needles as in George Ward's plan, or by deep Roentgen ray.

Yet we also have learned that practically the radiation never comes up to the possibilities which physics shows us it has. This I have well proved in a study of my own series. The untrained technician pays little attention to the meaning of screening or proper distance, but just puts the radium in anyhow and hopes for the best. Naturally he is at his worst when the surfaces to be radiated are irregular, as in large deep sloughs with a bore and depth of a couple of centimeters, or when the cancer is extending irregularly down the vaginal well. Then the instruments devised to hold the radium in the infiltrated fornix fail to keep it in the place where it is expected to be. Very often indeed will the careful technician find that he has radiated all the wrong places, and be reminded of Sampson's bizarre films showing radium in the cavity of the uterus far distant from the side wall where it was intended to be. I have no doubt the method of radiation adopted is not nearly as important as the detail with which it is carried out; the cure rates from well conducted clinics using different methods of radiation are essentially the same. The beginner will find it helpful at first to x-ray each case after placing the radium and packing it in place, in order to learn how much it has slipped or

fallen away from the position in which he intended it to be.

Nearly all radiologists at present employ the fractional dose method, repeating treatments not only successively to radiate all points desired but also to ray the greatest possible number of cells at the time they are dividing. Whether the treatments are daily or weekly depends upon what technique is followed. The filtration and the distance between the desired point of radiation and the capsule is usually the same in all treatments.

The combination of Roentgen ray and radium will improve results; when technical difficulties have made it impossible to apply radium in an ideal manner, and the capsule is not just where it should be, a broad beam of deep Roentgen ray may be a life saving measure. My own results prove that this is true. With a combination of radium and deep Roentgen ray the five year cure rate in eighty-two cases was 39.7 per cent, nearly double the number obtained from radium alone in a series approximately equal in size, treated just before we began to use Roentgen ray as part of the combination treatment. Neither series included any case that had been operated upon radically or even had had gland resections. The detailed report will soon be presented by Morton. (I operate radically and after preliminary radium treatment, in all the very good surgical risk cases where there are very early cancers.) The series just noted unfortunately is small. Were it very much larger, I much doubt if the history, other records and the follow-up could be nearly so good. My total cervical cancer series is only 750 cases, but the follow-up is complete on each case from time of treatment to date for twenty-four years. Nearly everything, height, weight, body measurements, all kinds of blood studies, basal metabolism, detailed family history, dietary history, and, in some cases, hormone studies have been made. Blood transfusions are routine.

The dosage of x-ray has changed very much during the course of the series, while



the x-ray men were trying to find the optimum dose, just as we had to do with radium. Our x-ray therapy is under the direction of Dr. Robert S. Stone, head of the x-ray department, who fortunately is also much interested in cancer therapy. The radium is given by members of my own staff.

In this last series, we used the Memorial Hospital technique for radium; most of the cases were treated with a 200 K.V. constant potential General Electric X-P tube, a few with our Sloan high-frequency generator operating at from 1000 to 1200 K.V. In general the pelvis was rayed through two  $10 \times 20$  cm. fields anterior and posterior. The number of Roentgens varied tremendously; in the very beginning a few cases had only 1000 per field, then quite a number had from 1600 to 2200 per field, and in the latter part of the series more than 3000 were given for each field. What neutron therapy will accomplish remains to be seen.

The time when the Roentgen ray treatment should be given has occasioned some debate. All the men in my group feel that it is optimum before radium and that the course should be completed before the radium treatments are begun. To my mind there is always a chance of causing metastases when dilating or otherwise manipulating a carcinomatous cervix that has not had Roentgen ray treatment previously or at least one treatment with radium plaques placed in the vagina against the cervix before dilatation.

When Stone began using the big 1200 K.V. machine and was trying to find proper dose levels, quite naturally many patients were made quite sick, sometimes so sick that we had to change our sequence and give radium before the Roentgen ray in order to get it into the treatment at all. Now, however, extremely sick patients are not common and the Roentgen ray is given first. It seems to me that fewer pelvic inflammations develop and become major complications when the Roentgen ray is so given. When such conditions develop

they may be extremely troublesome, disrupt or cause postponement of the treatments or keep the patient in bed for many weeks. That they do occur is everywhere evidenced in the literature.

In 1936 not only did Bowing and Fricke report major complications in 5.6 per cent of 495 cases, but Reiles and Fobe had peritonitis follow radium in six of their 100 cases.

The question of radium-resistant cells is most important and unfortunately is far from settled in spite of a tremendous and very confusing literature. That there are such cells is a fact—cells which have lived through tremendous doses of radium and of deep Roentgen ray and which are found at operation or autopsy. Some cancers which seem to be resistant to radium disappear under Roentgen ray. I wonder, therefore, whether these cells are actually resistant to radium or whether the real trouble is not a faulty radium treatment. I now consider a cell resistant only if it persists three months after the combined treatment of radium and Roentgen ray, and then only if it is situated in a part of the uterus where it could have been acted upon properly by both of these therapeutic agents. Most such cancers in my series have had transitional cells (Martzloff's classification) predominating, but most of the cancers in the entire series also have transitional cells predominating. Usually, however, the persistent cell in the tissue depths is more differentiated than that in the biopsy specimen from the surface of the cervix.

I have no way of calculating how frequently we find these cells, because the series is small and the technique is constantly changing. They were common findings in my earlier operations even though the cancers had received what then was called adequate radiation. We find them less commonly now, yet we occasionally find them (as we have said before) in spite of more than 5000 mc. hours (Memorial technique) and more than 3000 Roentgens from the 1000 K.V. tube to each of two

anterior and posterior fields each  $10 \times 15$  cm. given by a very competent technician who is also a physician. Within the next few months, I expect to make a detailed report of my findings.

Neither I nor my co-workers, Schulze and Morton, have ever been able to confirm from study of my cases the theories that the histologic cell type of the cell was a major factor in curability of the patient. Unfortunately the material is so small, as is that of nearly any other series available for study, that by the time the tumors are broken down into the same cell types and the same clinical grouping, i.e., the same estimated amount of anatomic invasion—using Schmitz's classification—the resultant subdivisions are too small to stand up under the mathematician's computations. There remain also other factors, such as the blood supply of the tumors, the type of vessels, their location, the type and condition and type of the patient, etc., points suggested by Norris, all of which defy evaluation.

And while not actually germane to this subject, the report of Cathie in February, 1939 is very interesting. This author attempted to ascertain in Manchester the possible relationship between the histologic grading of primary tumors and their metastases in a series of sixty-seven cases in which adequate biopsy material was available from the primary lesion and from dissections of tumor-bearing lymph nodes which drained the region. The cancers were from the mouth and genitalia and were correlated with their metastases in the regional lymph nodes of the neck and groin.

In thirty-four cases the grading of both primary and secondary growths was the same. In thirty-one cases the metastasis was more differentiated than the primary growth. In two cases it was less differentiated.

The question whether operation should be performed upon patients who are excellent surgical risks and whose cancers are small and definitely limited to the cervix

is less important now, when radiation has improved and is combined with intensive Roentgen ray therapy than it was when the most extravagant and absurd claims were made for the therapeutic action of radium. At that time my cure rate with radical operation after radium was twice what I obtained after radium alone in stage I and II (Schmitz) control cases. I am continuing the study chiefly to learn just what the combined therapy is accomplishing. I will abandon it when I find there are no radium-resistant cells in early cases which have been adequately irradiated and when the cure rate with the combined treatment equal that of my surgery.

Unfortunately the cancer student grows old equally fast with his patient and each change in radiation technique means another five years wait before one can tell what his change of technique has accomplished. The radiologist, when radium treatment was new, seemed to think that only the physicist was important, forgetting the pathologist and the fact that the changes they found in surface tissues might not be present in the deeper structures of the tumor.

Radical operation, however, is justifiable only when it can be done with little or no mortality and without any fistulas or other disagreeable major morbidity. In contrasting postoperative convalescence with the stormy period that now follows adequate Roentgen ray therapy, which is paramount to telling the woman she has a cancer, I am not certain which is the lesser of the two evils. Under no circumstances may the surgeon think that an ordinary pan-hysterectomy is, ever was, or ever can be a radical operation.

#### CONCLUSIONS

1. Present day cancer students may review with profit many of the fundamental investigations that were made by their predecessors long before the advent of radium into cancer therapy.

2. Radium never can be regarded as a "cure-all" for cancer of the cervix.

3. While there remains too much difference between the theoretical possibilities of radium treatment and what it actually accomplishes in cancer of the uterine cervix, it is not likely that the present day methods of application will be greatly improved.

4. The results obtained in leading clinics with radium therapy are essentially the same.

5. The combination of deep Roentgen ray and radium therapy gives a larger five-year cure rate than either treatment used alone.

6. Cancer students when reporting cures must not forget that some untreated cancers of the uterine cervix may allow the patient to live for years.

7. No definite relationship between curability, radium resistant cells and the histologic cell type of the primary tumor can be established in my series.

8. The ordinary panhysterectomy, with removal of the tubes and ovaries, is not a radical operation even for very early cervical cancers.



GRAVES holds it [cancer of the cervix] to have a life history of many years; the initial stage, of chronic cervicitis, being a long one, and the second, shorter, stage being marked by an actual cancerous change, a piling up of cancer-like cells which have not yet become invasive. Perhaps such lesions have not usually been recognized by pathologists, but it is more likely that surgeons have been content to repair rather than amputate the chronically inflamed and lacerated cervix.

From—"A Textbook of Surgery" by John Homans (Thomas).

# TOTAL VERSUS SUPRAVAGINAL HYSTERECTOMY

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OPERATIONS on the uterus for benign conditions constitute a large percentage of the major operative procedures on any gynecologic service. The type of operation to be performed in any given case depends not only on the pathologic condition, the patient's age, her marital state, the state of her general health and to some extent her wishes in the matter, but also on the experience of the surgeon and the results he has obtained with various types of operations in similar cases. In some cases more or less satisfactory results will be obtained with a variety of different operative procedures, but following some of these there may be the probability of future trouble which will require a second operation or frequent treatments. In my experience, in many cases in which trouble follows operation a cancer phobia develops to a greater or lesser degree. Many of them do not return to the original surgeon because they think he does not understand their case.

One of the most controversial points among gynecologists is whether to do a total abdominal hysterectomy or a supravaginal amputation in the majority of cases in which it is advisable to remove at least part of the uterine body. In all discussions on this subject it is freely admitted, even by ardent supporters of the more radical procedure, that statistics from the country as a whole will show a definitely higher mortality and morbidity when this operation is performed. This does not mean, however, that the operation is at fault, but simply that it is being attempted by some surgeons who are not familiar with the various steps of a difficult operation. I am satisfied that when total abdominal hysterectomy is done by competent surgeons in a large series of

cases, the end results are better, the morbidity is less and the mortality no greater than when a subtotal abdominal hysterectomy is done in a similar series of cases by the same experienced surgeons. For the occasional operator or for any surgeon who has not taken special pains to become thoroughly familiar with the technique of a total abdominal hysterectomy, my advice would be to continue doing the subtotal operation in a large majority of his cases even at the risk of leaving an infected cervix, which might require treatment or removal at a later date. A neglected infected cervix is a definite predisposing cause to complications; the most frequent of these is thrombophlebitis and the gravest are pulmonary emboli or the later development of cancer.

I do not agree with those who say that the only advantage of total abdominal hysterectomy over subtotal operation is the protection against the later development of cancer. If this were the case, I would not feel justified in advising the total operation as often as I do. Just what added danger there is of malignant disease developing in a cervical stump over the normal incidence of cancer of the cervix in a like number of cases is hard to determine. It is known, however, that cervicitis is a very common sequela to subtotal abdominal hysterectomy and that chronic irritation from infection is a definite predisposing cause of cancer. Statistics are very unreliable in such cases and vary a great deal in different countries and among different surgeons in any one country. The weight of statistical evidence, however, is that cancer occurs in probably not more than 1 or 2 per cent of cases in which a subtotal hysterectomy has been performed for benign conditions. Henriksen, in 940

cases of carcinoma of the cervix observed at the Johns Hopkins Hospital, found that carcinoma developed in the cervical stump in 2.3 per cent of them. At The Mayo Clinic, from July 1, 1930 to December 31, 1938, inclusive there were 1,489 cases in which a pathologic diagnosis of carcinoma of the cervix was made and of this number, sixty-five or 4.4 per cent were cases of carcinoma of the cervical stump. There is no doubt that this condition is reported much more frequently at the present time than it was formerly.

Von Graff reported on nearly 1200 cases in which cancer developed in the cervical stump and there is no doubt that many such cases are never reported. In most of the cases, as shown by C. H. Mayo and C. W. Mayo, the condition is not diagnosed until late and until the outlook for cure is not good. In a series of sixty-five patients who were treated for carcinoma of the cervical stump at the clinic and whom we were able to trace, we found that only thirteen, or 20 per cent, had lived five years. From January 1, 1910 to December 31, 1938, inclusive, we have seen 164 cases of carcinoma of the cervical stump. In twenty-four of these cases subtotal abdominal hysterectomy was performed at the clinic and in 140 cases it had previously been performed elsewhere. In 136 of these 164 cases, the malignant condition was recognized for the first time at least one year after the abdominal operation had been performed, and this interval, I think, should be accepted as evidence that the malignant lesion did not exist at the time of the supravaginal operation. Besides the cases of cervical cancer, we have seen many cases (more than 500) in which cervicitis with leucorrhea was sufficient to require treatment. In many of these cases there was no history of the occurrence of leucorrhea before the body of the uterus had been removed. Furthermore, recent investigation has shown definitely that cervicitis is frequently a focus for infectious arthritis, myositis, iritis and other disabling diseases. In addition to the danger

of cancer and cervicitis, one must recognize the danger of benign tumors, such as fibroids and cervical polyps, developing in a retained cervix. At the clinic we have operated on three patients for fibroids in retained cervixes and on many who had polyps.

The objections raised to the total operation, such as shortening of the vagina and a greater tendency toward prolapse of the vaginal vault, do not hold if the cervix is enucleated out of the vaginal vault and the latter is properly secured to the tissues from the base of the broad ligaments, uterosacral ligaments and round ligaments and if any relaxation or lacerations of the lower pelvic diaphragm are cared for at the same time or soon afterward. There is no doubt that obstetricians today are aware of the importance of puerperal gynecology, but Richardson has stated that "Recent reports from some of our best obstetric clinics reveal that late follow-up examinations disclose unsatisfactory conditions of the cervix and lower birth canal in 50 to 75 per cent of women who have borne one child or more." The contention that the total operation is a frequent cause of dyspareunia is unfounded. When this is a postoperative complaint, it is generally due to fixation of the ovaries to the vault of the vagina and to diminished vaginal secretion; this latter condition can be overcome by the use of a nonirritating lubricating jelly.

In reviewing the literature, it is interesting to find how infrequently physicians who have large gynecologic practices report cases in which complications or sequelae which require treatment occur after subtotal abdominal hysterectomy, whereas other physicians report seeing such cases frequently. It is not surprising that the former do not encounter cases of arthritis, neuralgia and iritis, but one would expect them to encounter an occasional case in which local disease had developed in the cervix itself. This can be accounted for, in part, by the fact that the patient fears that the operation was not

satisfactory and she therefore goes elsewhere for advice. The fact that subtotal hysterectomy had been performed elsewhere in 140 of the 164 cases of cancer of the cervical stump which we have seen at the clinic, lends strength to this argument.

Morbidity is frequently due to pelvic peritonitis of low grade, which these patients fortunately stand well, to thrombophlebitis and to adherent loops of small intestine in the pelvis. I have always thought that when a total hysterectomy is performed after surgical preparation of the vagina there is less chance of infection than there is when the subtotal operation is performed and the cervical glands are cut across and frequently are traversed with sutures. In many cases infection is already present. When the cervix is coned or is destroyed by cauterization, added protection from infection is not given as these procedures leave a sloughing region continuous with the operative field and peritoneum. Furthermore, such procedures do not protect against the occurrence of epithelioma of the cervix because this neoplasm starts on the portio vaginalis rather than in the cervical canal in most cases.

No matter which operation is performed, I am satisfied that a very important protection against subsequent trouble, not only while the patient is in the hospital but also for months or years afterward, is the care taken to prevent loops of small intestine from becoming adherent in the pelvis. This condition is the result of a pelvic infection of low grade, which is frequently caused by the use of drainage or occurs because all raw surfaces were not covered properly with peritoneum. If it is not possible to cover these raw surfaces in the ordinary way, it is advisable to utilize the sigmoid or appendices epiploicae. I have seen several instances of subacute intestinal obstruction months after a patient has left a hospital after what was regarded as a normal postoperative course and I have seen one case of complete obstruction fifteen years after a pelvic opera-

tion in which a loop of small bowel apparently had been adherent deep in the pelvis all that time. I am satisfied that many patients who die of peritonitis could be saved by early recognition of intestinal obstruction and freeing of a loop of small bowel adherent in the pelvis before infection spreads from the lumen of the bowel to the free peritoneal cavity.

In many cases of uterine fibroids in which the mass is not larger than a three months' pregnant uterus and in which the only symptom is menorrhagia, the advisability of performing a hysterectomy or treating by irradiation has to be considered. There is no doubt that there is legitimate ground for a difference of opinion if a subtotal hysterectomy is considered sufficient, but if there is any pathologic lesion in the cervix, I believe the best interests of the patient are served by removing the uterus completely. Radium and Roentgen therapy give excellent results with little inconvenience and hospital expense to the patient and practically no mortality. Burnam reported treatment by radium in 1800 cases without a death. One cannot, however, compare these statistics with surgical statistics because the former represent treatment in a very select group of cases. In all complicated cases, necessarily, treatment is by operation and many of the patients are exceedingly bad risks in whom operations are difficult. Moreover, in an occasional case in which the result is listed as good following treatment by radium months or even years before, subsequent treatment is required for leucorrhea, menorrhagia, adnexal trouble or malignancy. At least once a year I see a case in which carcinoma of the body of the uterus has occurred after the use of radium therapy. Statistics show that in an unselected group of cases in which operation is advisable and is performed by a member of the visiting staff of most accredited hospitals the mortality rate associated with subtotal abdominal hysterectomy is about 4 per cent and that asso-

ciated with total abdominal hysterectomy is about 6 per cent.

There are reports of cases in which cancer developed in the vault of the vagina after a total abdominal hysterectomy, but I never have heard of such a case in which carcinoma of the vault of the vagina followed a vaginal hysterectomy. It would be impossible to prove but I have seen so many cases in which a total abdominal hysterectomy was supposed to have been done and in which some cervical tissue was left that I believe that such cases should be listed as cases in which carcinoma developed in the cervical stump rather than as cases in which the growth was vaginal in origin.

From January 1, 1934 to December 31, 1938, inclusive, hysterectomy was performed for benign conditions in 3,149 cases at the clinic. In the 1,776 cases in which total abdominal hysterectomy was performed, twenty-two or 1.2 per cent of the patients died; in the 766 cases in which subtotal abdominal hysterectomy was performed, seven or 0.9 per cent of the patients died, and in the 607 cases in which vaginal hysterectomy was performed, nine or 1.5 per cent of the patients died. During the years 1936, 1937, and 1938, I performed 784 hysterectomies with six deaths, or a mortality of 0.76 per cent; 196 of these were vaginal hysterectomies with one death, a mortality of 0.51 per cent.

In recent years I have become more and more convinced that a total hysterectomy is advisable in most cases in which it is necessary to remove any of the uterine body of women who have been delivered of children by the vagina and who are close to or at the menopausal age, provided the surgeon is familiar with the technique of such an operation and can complete it within an hour. I am satisfied that the three most important considerations in a low operative mortality are: (1) a well given anesthetic; (2) adequate exposure; and (3) no unnecessary delay in completing an operation. Few abdominal operations

should keep a patient on the operating table more than one and a half hours.

There is no doubt that spinal anesthesia, as given today by specialists in this field of therapy, is a relatively safe procedure, but I do not feel that it is as safe as a well given inhalation anesthetic by an expert with a modern anesthetic machine and the various gases that are now used under direct control. If I did not have an excellent anesthesiologist, I certainly would use spinal anesthesia much more often than I do. I am satisfied that spinal anesthesia always makes an operation easier for the surgeon but a little more dangerous for the patient.

In any consideration of hysterectomy it is also necessary to consider the disposition of the adnexa. Some surgeons feel that if the uterus is to be removed there is little to be gained by saving the tubes and ovaries, whereas others feel that the ovaries should be saved whenever possible. If the patient is close to or past the menopausal age, there can be little difference of opinion. Most surgeons agree that cutting the infundibuliform ligament close to the brim of the pelvis and total removal of tube and ovary on both sides are indicated if the uterus also is to be removed. The Fallopian tubes are of no use if the uterus is removed, but the ovaries are of definite value to the patient still in the child-bearing period of life. My practice has always been to save normal ovarian tissue when possible in young patients when operating for benign conditions. I would sooner consider the possibility of a second operation for some ovarian condition than to remove both ovaries of a woman less than 40 years of age. In recent years I have adopted the practice of removing the Fallopian tubes whenever I have to do a hysterectomy. I never could see any advantage in leaving them and I frequently have on my service patients in whom a second operation is made necessary on account of tubes that have been left following a hysterectomy. If care is taken in their removal there should be no interference with adequate blood supply to the ovary. The tubes develop

along with the uterus from the Müllerian ducts and their principal blood supply comes from the terminal branches of the uterine arteries. When these vessels are cut the ovarian vessels have to supply the tubes as well as the ovaries. They are able to do this all right but with the slowing of circulation clotting often takes place in the venous plexus in the mesosalpinx and this may well be the starting point of a pelvic thrombophlebitis. On my own service I certainly have had less trouble with pulmonary embolism and other less serious complications since I have been doing the more radical operation. As far as I can tell, the ovaries function normally in just as high a percentage of cases.

Most authors who advise the more frequent use of subtotal hysterectomy have figures to show that the bladder, ureters and bowel are less frequently injured when the less radical operation is performed. The only reason I can see for this is that some surgeons who are doing total abdominal hysterectomy do not see accurately what they catch with each forceps or include with each stitch. In the technique that I use, I ligate the uterine vessels at the same point in all cases of benign lesions no matter whether I do a total or a subtotal hysterectomy. The only difference is that I have to tie separately an extra branch that goes to the cervix on each side in all cases in which I perform a total hysterectomy. Abnormally situated ureters are occasionally noted, but as a rule they run a normal course unless pressed upon by uterine or ovarian tumors. The way to avoid them is to keep close to the uterus. In all cases of doubt it pays to isolate them before attempting to control deep pelvic bleeding, and in peritonealizing the raw surface all stitches should be superficial.

Injuries to the bladder are probably most often due to stripping the bladder from the cervix by blunt or gauze dissection rather than by sharp dissection. This is especially true in cases in which the uterine lesion is complicated by pericervicitis. Personally,

I prefer a sharp knife to scissors for this part of the operation.

#### TECHNIQUE

The especially long instruments and the Mayo fibroid hook which I use for performing hysterectomy are shown in Figure 1. A Kocher hemostat is first placed close to the right side of the uterus; it includes the proximal parts of the right round ligament, the right Fallopian tube, the right utero-ovarian ligament and the upper part of the right broad ligament. Another hemostat is placed on the right round ligament just distal to the first forceps; the round ligament is cut between them and the peritoneum is cut on each side of the round ligament for a distance of  $1\frac{1}{2}$  or 2 inches (3.8 or 5 cm.). (Fig. 2.) The fimbriated end of the right Fallopian tube is now grasped with forceps and the tube and ovary are thoroughly inspected. If it is decided to save the ovary but remove the tube, I catch the vessels close to the tube with one or two clamps and then cut the ovary free from the uterus by cutting the utero-ovarian ligaments between clamps. I like at this time to tie securely the end of the round ligament, the utero-ovarian ligament and the various vessels secured by forceps after removal of the tube. The various steps of the operation as described are now repeated on the left side of the uterus, but in most cases the ovary is also removed on the left side as it is less liable to cause postoperative discomfort, but if the left ovary is the better of the two, it is saved and the one on the right side is removed. Traction is now made on the forceps placed on each side of the uterus. The peritoneum is cut in front and the bladder is freed from the cervix and vault of vagina by sharp dissection. (Fig. 3.) As a rule, it is necessary to ligate one small artery in the vesico-cervical fold on each side. By continuing traction on the uterus and drawing it down over the symphysis pubis, the uterosacral ligaments are exposed. These ligaments are then cut from the posterior surface of the cervix. At this time, I also like to cut the



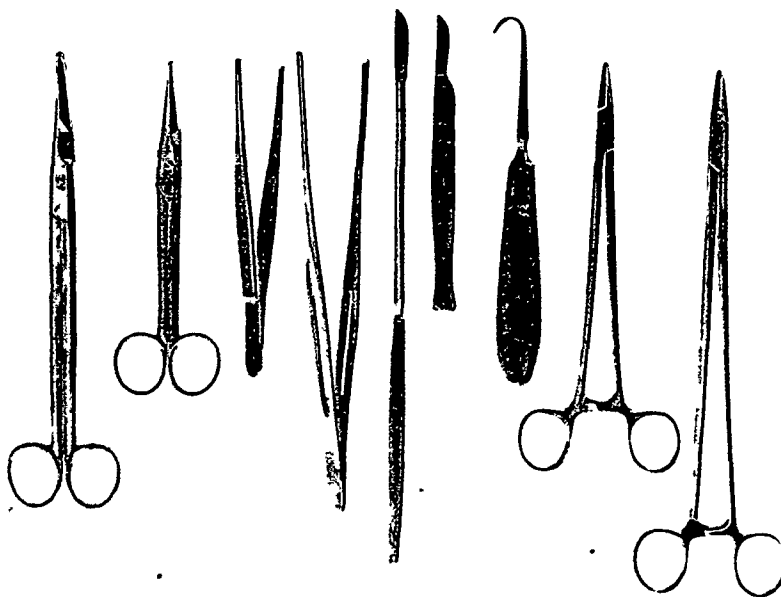


FIG. 1. The Mayo fibroid hook and long-handled instruments are a definite help in most cases.

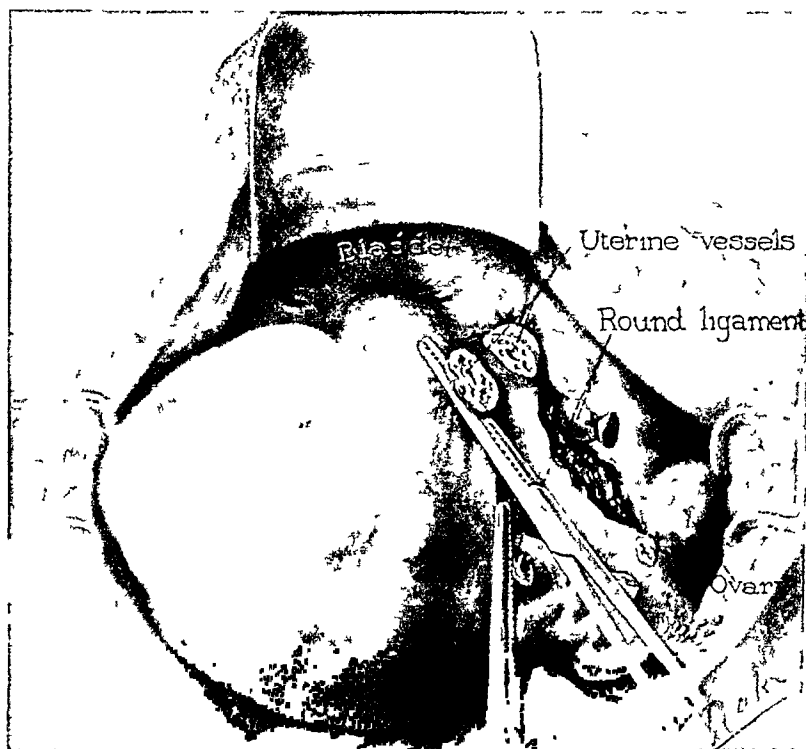


FIG. 2. Cutting through broad ligament; stumps of uterine vessels round ligament and utero-ovarian ligaments have been ligated.

peritoneum across the posterior surface of the broad ligament.

The uterine vessels and the cardinal

secured is the same whether one is doing a total or subtotal operation. The only difference is that if a subtotal operation is

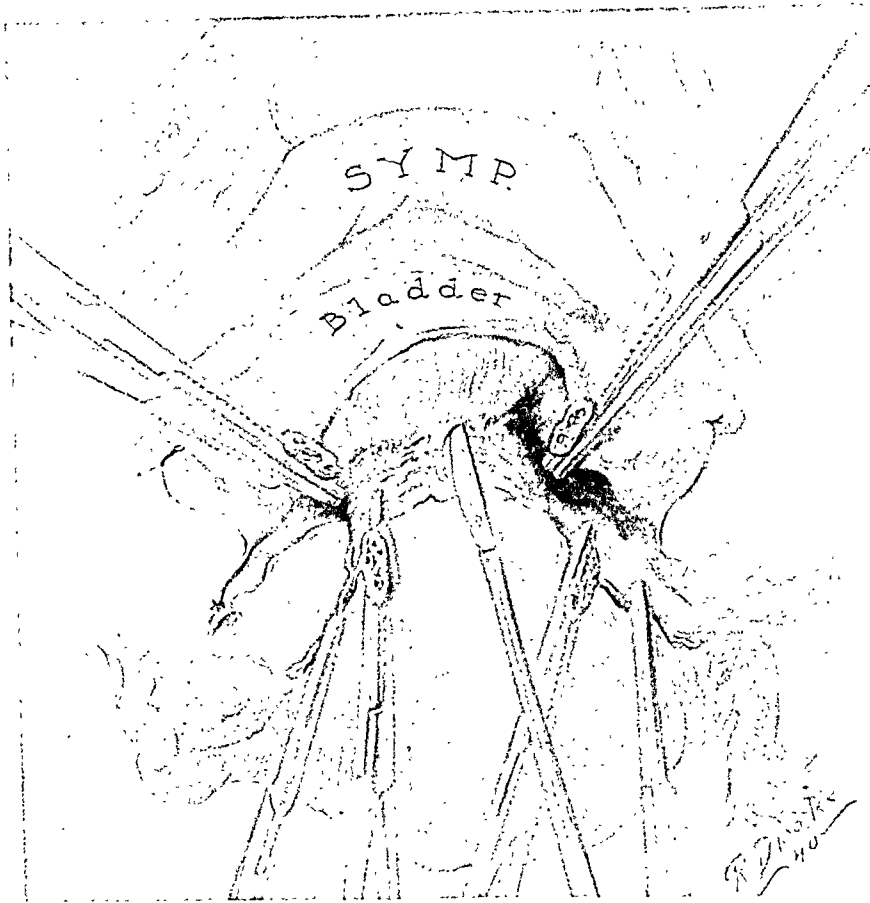


FIG. 3. Separating bladder from cervix by sharp dissection; uterine vessels doubly clamped at right angles to cervix.

ligament in the base of the broad ligament are now caught at about the level of the internal os with three Kocher hemostats that are applied almost at a right angle to the cervix, and the tissues are cut between the upper and middle forceps. If this technique is followed, I do not believe it is necessary to isolate the ureters as there is no chance of injuring them if the forceps catch right up to the cervical tissue. It is only in the exceptional case in which some bleeding occurs deep in the base of the broad ligament or along the side of the vagina that I feel that it is necessary to locate the ureters before controlling the bleeding. I do not believe that inserting ureteral catheters before starting the operation is a necessary or good practice. The point at which the uterine vessels are

contemplated the cervix is cut across at the level at which the uterine vessels are clamped and the cervical canal is closed by two or three stitches, whereas when a total hysterectomy is contemplated the pericervical tissues are cut and the cervix is enucleated from the vaginal vault. If the surgeon works close to the cervix in this part of the dissection there is no danger of injury to ureter, bladder or rectum. Constant traction on the uterus by means of Mayo hooks and the use of a knife with a long handle or a long pair of scissors make this part of the operation easy. (Fig. 4.)

As soon as the vagina is opened I insert a strip of gauze about 2 inches wide and 12 inches long, which has been dipped in tincture of merthiolate. This is left in place until the third or fourth postoperative day.

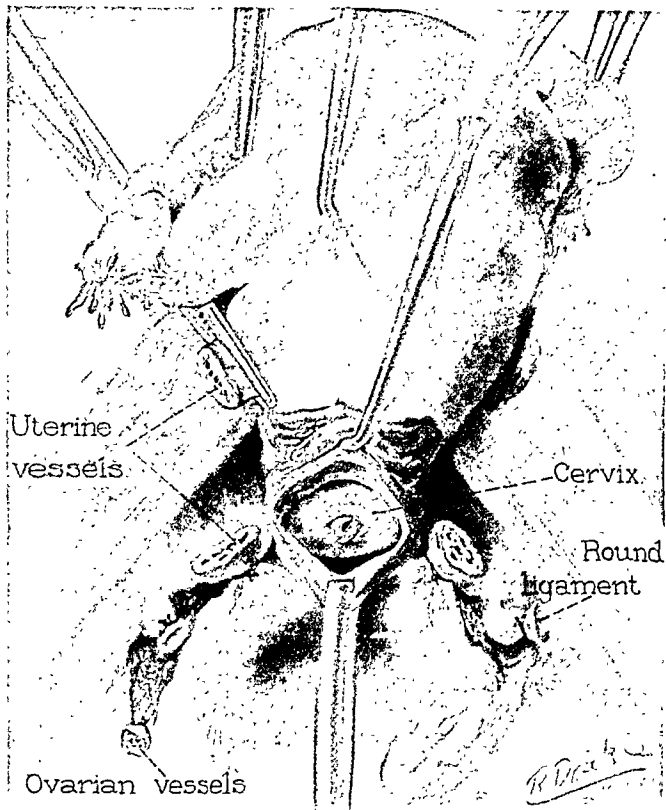


FIG. 4. The uterus freed on both sides, a hook is inserted in the posterior surface of the cervix to make traction; the vault of the vagina is cut posteriorly and a tenaculum is placed on posterior wall of the vagina; gauze soaked in tincture of merthiolate is inserted into the vagina before the operation is started.

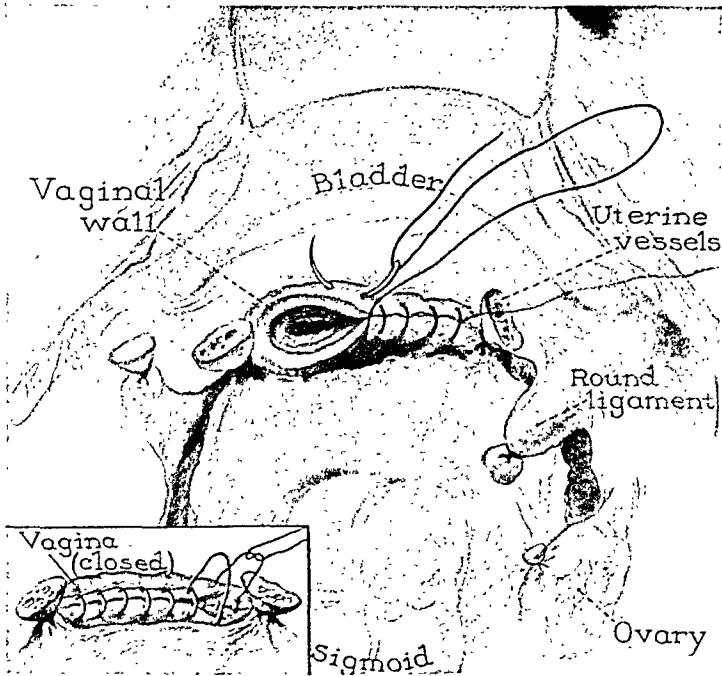


FIG. 5. Closure of vagina, showing method of insertion of two rows of sutures.

The vault of the vagina is closed with a continuous mattress suture that rolls the cut edge of the mucous membrane into the

the vagina and I think it is important to make a wide approximation of the round ligaments (if possible, overlapping them) to

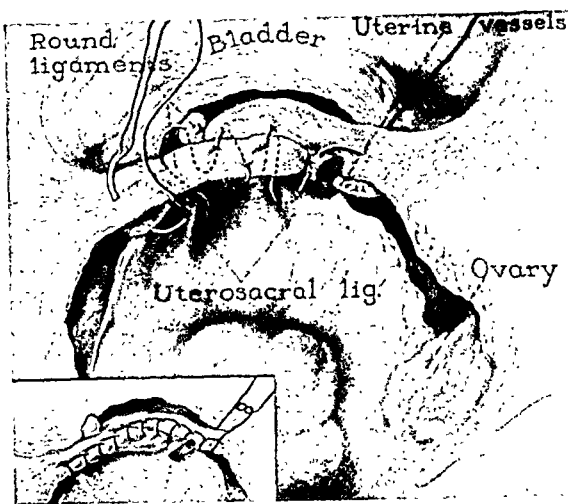


FIG. 6. Fixation by two rows of sutures of round ligaments, stumps of uterine vessels, uterosacral ligament and vault of vagina.

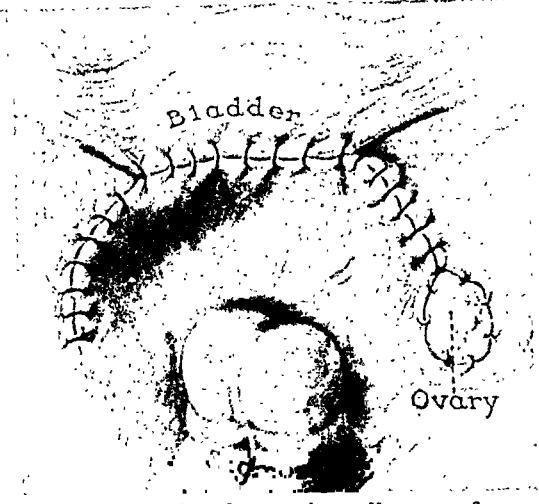


FIG. 7. Completed operation; all raw surface covered with peritoneum; ovary partially buried in peritoneum and fixed well up on side of pelvis.

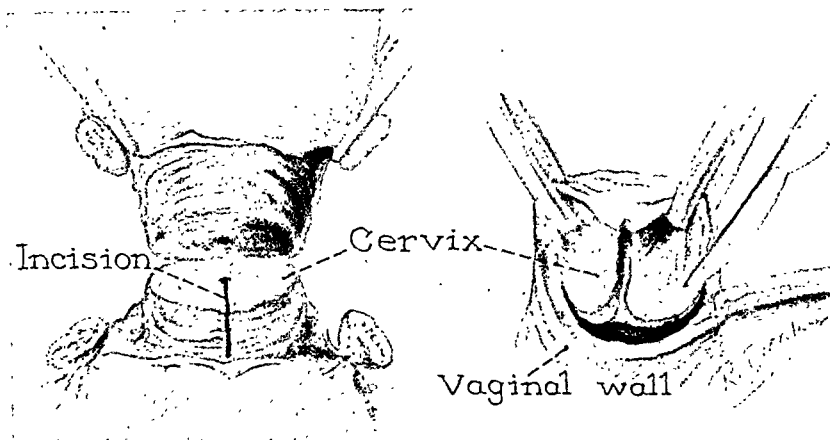


FIG. 8. In cases in which the operation is difficult the body of uterus is removed as in subtotal hysterectomy, the cervix is split posteriorly and removed separately.

vaginal canal. It is also a good hemostatic suture. To close the vagina further the peritoneum and uterosacral ligaments are brought upward from behind and placed over the vault of the vagina by a continuous suture. (Fig. 5.)

The uterine vessels and the cardinal ligament are ligated en masse by a stick tie that secures some of the vaginal wall, but an attempt is made not to reach the mucous membrane of the vaginal canal. The round ligaments are now secured to the vault of

the tissues in the base of the broad ligaments, the stumps of the uterine vessels and the uterosacral ligaments. (Fig. 6.) All raw surfaces are now covered by peritoneum, and the ovary, if saved, is partly buried between the folds of the broad ligament well up on the side of the pelvis rather than fixing it to the vault of the vagina as is so often done. (Fig. 7.) If the left ovary is saved, special care should be taken to prevent it from becoming adherent to the sigmoid. If there has been an old

pelvic inflammatory condition, it is often impossible to close the peritoneum in the usual way, and it is then frequently necessary to obliterate the cul-de-sac of Douglas more or less and cover the raw surface by stitching the sigmoid and appendices epiploicae to the posterior surface of the broad ligaments and posterior surface of the vagina.

In many cases in which it is expedient to remove the cervix, especially where there is an old pelvic inflammatory condition, it often simplifies the operation to perform a supravaginal amputation first and then to split the cervix posteriorly and shell it out from the vault of the vagina under direct vision. (Fig. 8.)

In the majority of cases it is advisable to remove the appendix at the same time, as this procedure adds little if any risk to the operation and occasionally saves the patient from another intervention.

The use of drains either through the abdominal incision or through the vagina, when not necessary, is a very definite added danger to any pelvic operation and as it is seldom necessary to operate for acute pelvic conditions it is rare, indeed, that any drainage is necessary. For several years, I have never used any abdominal or vaginal drainage even in operations for old pelvic inflammatory conditions or Wertheim operations for carcinoma of the cervix. If a tubo-ovarian abscess is ruptured during removal, the pelvis is washed out with physiologic saline solution and a tube drain is carried down to the peritoneum but not into the peritoneal cavity, when the wound is being closed. There is no doubt that the peritoneum can resist infection better than the soft tissue of the abdominal wall, and if a drain is inserted into the peritoneal cavity it causes a definite increase in post-operative adhesions and in the possibility of obstruction, and no good purpose is served. Whenever an infection becomes chronic it is a definite indication that the patient has a good resistance to that particular infection.

#### PREOPERATIVE AND POSTOPERATIVE TREATMENT

In many cases in which there is a history of menorrhagia the patients are exceedingly poor surgical risks on account of the secondary anemia that has developed. In these cases a preoperative transfusion of whole blood definitely decreases the risk, but my practice for some years has been, if the patient is able to be up and around the greater part of the day, to have her blood typed and, if necessary, a transfusion can be given any time after the operation. Since I started using a 6 per cent solution of acacia (about twenty years ago) in any case in which the blood pressure remains low following operation or the patient exhibits any signs of shock during the operation, I have used whole blood very seldom except when the concentration of hemoglobin has been less than 5 Gm. per 100 c.c. of blood.

#### CONCLUSIONS

1. More than 50 per cent of women who have borne one child or more have an unsatisfactory condition of the cervix and lower part of the birth canal.
2. Statistics from most hospitals show that subtotal abdominal hysterectomy is a safer operation than total abdominal hysterectomy.
3. Experienced surgeons can develop a technique by which a total abdominal hysterectomy can be performed as safely as the subtotal operation and with a lower morbidity.
4. The bladder, bowel or ureters will not be injured if the surgeon sees what is included in the grasp of each hemostat or in each suture.
5. Danger of cancer developing in the cervical stump is not the only reason for its removal, but cancer developing at this site is more frequently reported than formerly.
6. If a total abdominal hysterectomy is properly performed there is no tendency to prolapse of vaginal vault or shortening of the vaginal canal.

7. Neglect to repair the perineum often accounts for an unsatisfactory result following abdominal hysterectomy.

8. Morbidity is most frequently due to thrombophlebitis, low-grade pelvic peritonitis and firm adhesions of loops of small intestine deep in pelvis.

9. In my opinion spinal anesthesia makes any abdominal operation easier for the surgeon but a little more dangerous for the patient.

#### REFERENCES

1. BURNAM, C. F. Evaluation of irradiation in the treatment of uterine fibroids. *Am. J. Roentgenol.*, 37: 234, 1937.
2. HENRIKSEN, ERLE. Quoted by Richardson, E. H.<sup>4</sup>
3. MAYO, C. H., and MAYO, CHARLES, 2nd. Carcinoma of the cervical stump following subtotal hysterectomy. *Ann. Surg.*, 93: 1215, 1931.
4. RICHARDSON, E. H. Total versus subtotal abdominal hysterectomy in benign uterine disease. *Am. J. Obst. & Gynec.*, 30: 237, 1935.
5. VON GRAFF. Quoted by Richardson, E. H.<sup>4</sup>



IN 1809 Mary Crawford rode 60 miles on horseback, that Ephraim McDowell of Danville, Kentucky, might attempt the removal of an ovarian cyst so large that her abdomen hung well down towards her knees. From—"A Textbook of Surgery" by John Homans (Thomas).

# THE CHOICE OF OPERATION FOR UTERINE PROLAPSE\*

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THE management of uterovaginal prolapse is a problem which has commanded the attention of gynecologists and surgeons for many years, and yet there is no unanimity of opinion in regard to the surgical treatment of this lesion. This may be proved by the fact that innumerable procedures have been proposed for the correction of this disorder. Admittedly, the problem is a complex one and no one method is adaptable to all cases. The best results, therefore, are obtained when patients are individualized and when the surgeon views the situation with an open mind, choosing the operation best suited for the particular individual under consideration.

Uterine prolapse is usually classified in three degrees: the first degree, when the cervix appears at the vulva; the second degree, when the cervix is extruded; and the third degree, to which the term *procidentia* is applied, when the entire uterus appears in the outside world. To a certain extent the treatment is governed by the degree of prolapse of the organs. This may be medical or conservative and surgical or radical. The medical measures are concerned with the use of pessaries and tampons, which necessarily give but temporary relief. The pessaries, however, are of value in caring for certain patients with the lesser lesions, and their employment may allow these patients to continue through the child-bearing period before resorting to operative procedures. Vaginal tamponade with gauze and lamb's wool tampons is practically never used in the modern management of this condition.

Three factors, among others, are outstanding in the determination of what

operative method should be chosen in surgically treating uterine prolapse: first, the age of the patient; second, the possibility of future pregnancies; and third, as previously mentioned, the extent of the prolapse.

Extensive prolapse during the child-bearing age, because of its great discomfort, demands surgical attention. In this instance it is advisable so to reconstruct the parts that there will be no interference with future childbirth. This may be satisfactorily done by curetting the uterus, performing a bilateral trachelorrhaphy, an anterior colporrhaphy, a colpoperineorrhaphy, and, through an abdominal incision, shortening the uterosacral ligaments and performing a round ligament suspension of the uterus. The Simpson type of suspension gives satisfactory results. In this type the round ligaments are drawn through the internal rings to obliterate the spaces on the sides, and are attached to the under-surface of the anterior sheath of the rectus muscle on each side. When the round ligaments are markedly attenuated the Olshausen suspension is adequate. Here the round ligaments, close to the uterine horns, are fixed to the anterior abdominal wall by fine silk sutures. This operation has the advantage of using the strongest portion of the round ligament where it is picked up close to the uterus; it has the disadvantage of leaving a dead space on each side, but this may be overcome by closing this area with a purse-string suture of fine silk. During the child-bearing age, the cervix should not be amputated for three reasons: (1) because of the dystocia it will occasion in future labors; (2) because it is responsible for the early termination of

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pregnancy in a number of instances; and (3) because it may result in sterility. Obviously, abdominal fixation of the uterus

after operation, and, in order to overcome them, extensive vaginal dissection was necessary.

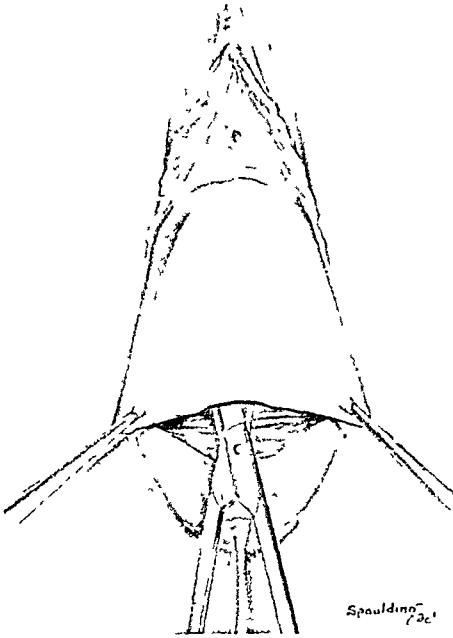


FIG. 1. The cervix is steadied by a Jacob's volsellum. A transverse incision is made in the anterior vaginal wall, in the region of the internal os. The vagina is separated from the bladder with scissors.

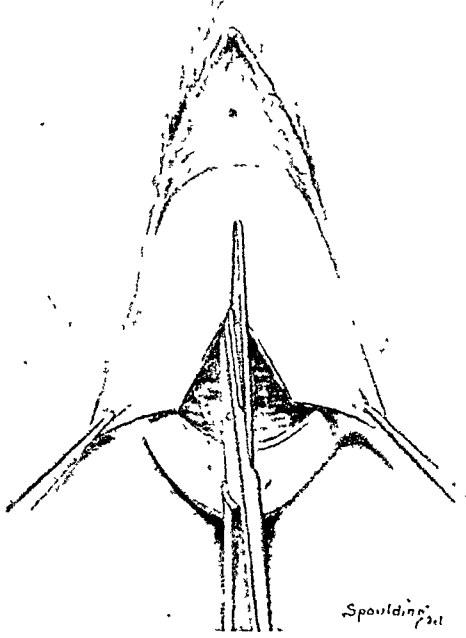


FIG. 2. The anterior vaginal wall is incised in the median line by scissors, exposing the bladder.

during the child-bearing age should not be considered because of the severe dystocia which will result therefrom.

After the menopause, or when child-bearing is no longer a factor, certain surgeons treat uterine prolapse by amputating the cervix, performing an anterior and posterior colporrhaphy, a perineorrhaphy, and a fixation of the uterus to the anterior abdominal wall. I personally have never favored abdominal fixation in the treatment of prolapse, since, if child-bearing is not considered, I believe better results are obtained by choosing one of the methods which may be carried out entirely through the vagina. Moreover, this lessens the risk of operation, since it obviates the necessity of doing a laparotomy. Two of the largest cul-de-sac hernias which I have encountered were seen in women who had had prolapse treated by vaginal plastics and abdominal fixation of the uterus. These occurred between ten and fifteen years

When dealing with women who have passed the menopause and with very old women, one of the vaginal procedures is usually resorted to, an abdominal incision being made only in rare instances. The reasons for so doing are that the vaginal operations increase the operability rate because of lessened morbidity and mortality; and because, in women whose child-bearing function has been terminated, the uterus and broad ligaments may be used to construct the support which elevates the prolapsed uterus and bladder in the pelvis. An adequate repair of the pelvic floor should accompany all vaginal operations for prolapse.

The vaginal operations in common use are:

1. Interposition of the uterus (Watkins-Schauta-Wertheim).
2. Vaginal hysterectomy (Mayo or Price-Kennedy).
3. High vaginal fixation of the uterus.
4. Colpectomy (Subtotal or total).



5. Interposition of the cervical stump in inversion of the vagina following supravaginal hysterectomy.

tion of the uterus would make their treatment difficult and arduous. The operation finds its greatest field of usefulness

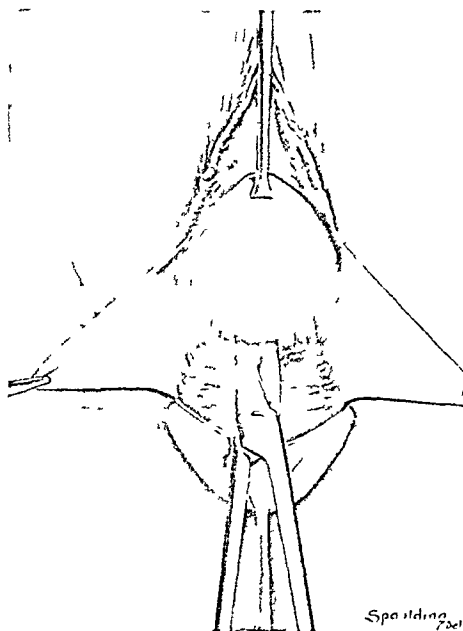


FIG. 3. The bladder is separated from the anterior vaginal wall and from the cervix by cutting the bladder pillars, thus exposing the basis of the broad ligaments.

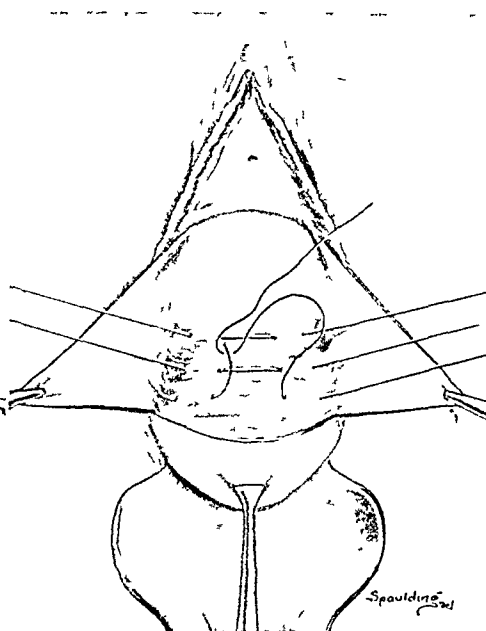


FIG. 4. Three sutures of No. 2 chromic catgut are placed in the bases of the broad ligaments and left untied.

6. Manchester operation (Donald-Fothergill).

7. Operation for hernia of the cul-de-sac of Douglas.

#### INTERPOSITION OF THE UTERUS

##### (Watkins-Schauta-Wertheim Operation)

This procedure, which was first performed by Watkins<sup>13</sup> of Chicago, in January, 1898, is frequently referred to in the literature as the Watkins-Schauta-Wertheim operation. Watkins performed it more than a year before Schauta or Wertheim, and should, therefore, get the credit for its establishment.

This procedure should not be advocated in women who are still in the fertile period. It is obvious that it would make delivery through the birth canal hazardous. Furthermore, if it is performed in young women, myomas of the uterus may subsequently develop, and the abnormal posi-

tion of the uterus is normal in size, about 3 inches, (7.5 cm.) in length, and when it is not friable. It is best employed when there is a first or second degree prolapse with a large cystocele. If attempted in the presence of a senile, atrophied uterus, recurrence will be common, since the bladder, by its greater weight, will force the interposed uterus through the vulva. Again, recurrences will be more common if the procedure is used with a third degree prolapse.

A great deal has been written about the bladder disturbances which may follow this operation, but these have not occurred in my experience. If the bladder is freely separated from the anterior vaginal wall, if the uterovesical ligament and the bladder pillars are cut and the bladder is completely separated from the uterus, after the interposition of this organ the bladder will lie smoothly and not in folds on the superior and posterior surfaces of the uterus. No discomfort, as a rule, will be

encountered. If, on the other hand, the bladder pillars remain attached and the fundus of the uterus is interposed, there

fact that if recurrence takes place, the organ is still present and can be utilized in an attempt to overcome the defect.

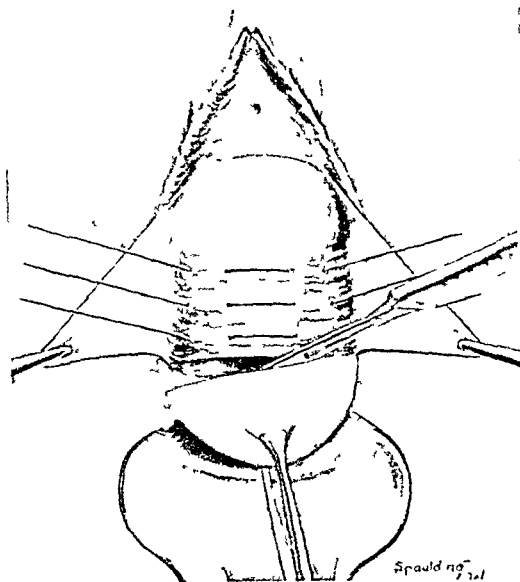


FIG. 5. The cervix is amputated below the level of the lowermost broad ligament suture.

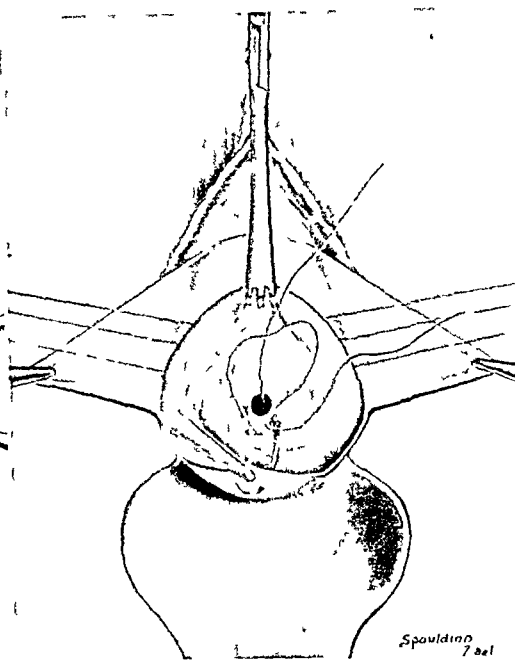


FIG. 6. The cervix is reconstructed by attaching the vaginal wall to the cervical canal, starting in the median line posteriorly.

will be constant pull on the bladder, giving rise to distressing bladder symptoms.

In my statistics of uterine prolapse and cytocele I find that I have used the interposition operation more than any other method. By observing the criteria above mentioned, I have obtained satisfactory results, although it is possible to observe late recurrences if one's patients are followed carefully. Recently I saw two women, one of whom I had observed for fourteen and the other for eleven years. Both had obtained excellent results following this intervention. However, in the course of time the uterus had atrophied, so that in each instance it became the size of an English walnut, and recurrence was noted. This recurrence can be easily corrected by performing a vaginal hysterectomy and using the broad ligaments as a support for the bladder. In the treatment of uterine prolapse, operations which retain the uterus have an added advantage in the

#### VAGINAL HYSTERECTOMY

(Mayo or Price-Kennedy)

Vaginal hysterectomy for uterine prolapse has been done extensively in this country during the last two decades. More recently, two clinics, the Michael Reese of Chicago<sup>2</sup> and the Johns Hopkins,<sup>4</sup> have reverted to other types of operations which conserve the uterus. In my opinion vaginal hysterectomy should be reserved for those cases in which there is uterine or cervical pathology, and in which bleeding is present. The operation may be performed with sutures or with clamps.

Vaginal hysterectomy with sutures was popularized by Charles H. Mayo. In this type of operation the entire uterus is removed, the broad ligaments are approximated and interposed between the bladder and the vagina, after resection of the excess of the anterior vaginal wall. A very important part of the intervention, and one

which is usually not stressed sufficiently, consists of the approximation of the uterosacral ligaments in their entire length by

toward the urinary meatus, is resected; and the anterior vaginal wall is approximated by interrupted sutures of silkworm gut or

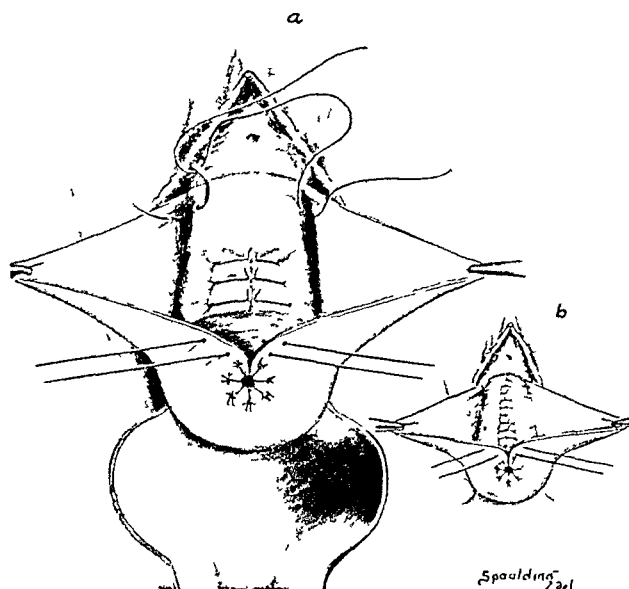


FIG. 7. *a*, the cervix has been reconstructed, the cervical canal is patent and roomy. The three broad ligament sutures have been tied. A series of interrupted sutures are placed in the musculofascial tissue, to the sides of the bladder, to overcome the cystocele. In insert, *b*, these sutures have been tied.

interrupted sutures of catgut or fine silk in order to prevent herniation of the cul-de-sac of Douglas, which frequently occurs when this condition is neglected. It is a wise plan to isolate the uterosacral ligaments, to clamp and cut them, and to replace the clamp on each side by a suture ligature at the start of operation. Like all others, this method is followed by a posterior colporrhaphy and a perineorrhaphy.

In the older group of women, when it is deemed advisable to remove the uterus in the treatment of uterine prolapse, vaginal hysterectomy may be done by means of clamps following the Price-Kennedy technique. This method is especially useful when the time element is a factor. By the use of special clamps, devised by Kennedy, the uterus may be removed in the course of a few minutes, an average time being about five minutes. Following this, a wide V in the anterior vaginal wall, with the point

prepared silk. On an average this entire procedure takes less than fifteen minutes. The clamps are removed at the end of seventy-two hours, and the non-absorbable sutures from the anterior vaginal wall at the end of two weeks. Two and one-half to three weeks after the hysterectomy and anterior colporrhaphy, the perineum may be repaired. This is usually done under local anesthesia, thus dividing the operation into two stages, each stage taking but a short time to perform. This intervention is well borne by feeble women who would not stand a long operation. Its one disadvantage is that it necessitates hospitalization for four and one-half to five weeks, but this in itself is not a serious drawback when one considers the good results obtained. The results following this operation are gratifying; the vaginal vault is pulled up high in the pelvis, higher than it is possible to bring it by means of sutures, and recur-

rences are said to be very rare. I personally have not observed any during the period of time I have employed it.

In the woman who is in good condition,

this method of great value in recurrent prolapse where a previous vaginal plastic operation and an abdominal fixation of the uterus had been done.

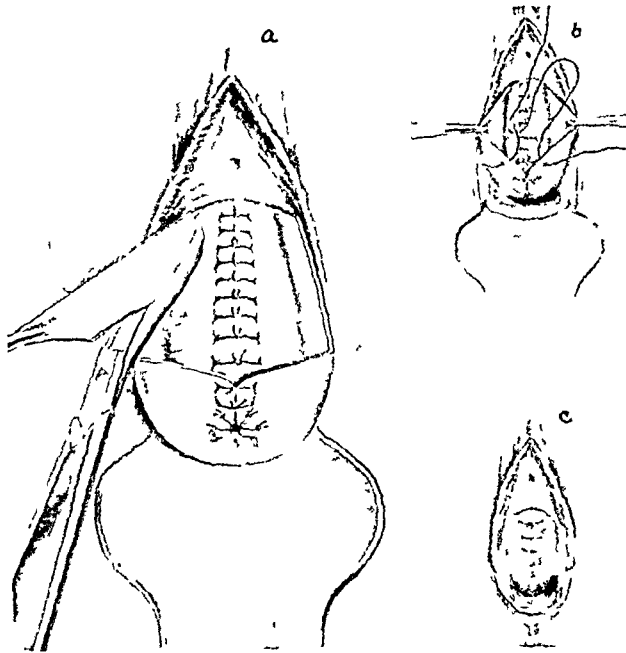


FIG. 8. *a*, the excess of the vaginal flap on each side is resected and the anterior vaginal wall is closed from below upward, *b*, The vaginal wall is entirely closed, *c*, The cervix is now well back in the pelvis, the fundus is in forward position and the cystocele has been overcome.

when the uterus has to be sacrificed, I am apt to use a modification of the Mayo technique and a colpoperineorrhaphy because the patient usually can be discharged from the hospital at the end of two weeks.

#### HIGH VAGINAL FIXATION OF THE UTERUS

This procedure consists of making an inverted T-shaped incision in the anterior vaginal wall, separating the bladder from the vagina and from the uterus, and suturing the anterior surface of the uterus to the anterior vaginal wall after removing, by resection, the excess of this wall. The cervix may or may not be amputated, depending upon the length of the uterus. This method raises the uterus in the pelvis and completely overcomes the cystocele. With the addition of a proper repair of the pelvic floor, adequate results in first and second degree prolapse are obtained. I have found

In a patient recently treated, the uterus had previously been fixed to the abdominal wall and the cervix appeared outside of the vulva for about 3 inches (7.5 cm.). The lower third of the uterus was amputated, the middle third was sutured to the anterior vaginal wall, while the upper third remained attached to the abdominal wall. This patient obtained a good result and has remained cured for a period of time sufficient to attest to the value of the operation. In this type of case the interposition operation or the Mayo vaginal hysterectomy are not considered, because of the increased difficulty in attempting to separate the fundus of the uterus from the abdominal wall through a vaginal incision.

#### COLPECTOMY SUBTOTAL OR TOTAL

Subtotal colpectomy or LeFort operation is practically devoid of shock when per-

formed under local anesthesia. It is indicated in old, feeble patients, who have a total inversion of the vagina and an atrophied uterus, or total inversion of the vagina following subtotal or total hysterectomy. It should not be employed when menstruation still exists, nor in the younger group of women. Its one drawback is that it obliterates the vagina, but this factor is not especially important in the older group of patients. It is, therefore, applicable to those whose ages make sexual congress unimportant.

For the very extensive inversions of the vagina total colpectomy, an operation proposed by Dujarier and Larget, forms a satisfactory method of treating this condition. In either case a small perineorrhaphy, approximating the levator ani muscles in the median line, forms an added barrier against recurrence. The final result is a small, shallow vagina. In my hands this operation has proved to be most successful, and considerable comfort has been obtained by the group of older patients on whom it was performed.

#### INTERPOSITION OF THE CERVICAL STUMP IN INVERSION OF THE VAGINA FOLLOWING SUPRAVAGINAL HYSTERECTOMY

Occasionally, one may encounter a younger woman who has had a supravaginal hysterectomy with total inversion of the vagina, including the cervical stump. Because of the age of this group of patients it is inadvisable to close the vagina, as in colpectomy. An operation which has served me well may be performed in this group. The anterior vaginal wall is opened by an inverted T-shaped incision, the vagina is separated from the bladder, the bladder is raised from the cervix, and the cervical stump is interposed between the bladder and vagina after resecting the flaps of anterior vaginal wall. A colpoperineorrhaphy is then performed. The three women upon whom I have operated by this procedure have been under observation for a considerable period of time, the results

have been gratifying and there has been no interference with marital relations.

#### MANCHESTER OPERATION

(Donald-Fothergill)

The principle on which the Manchester operation is based consists of approximating by sutures the overstretched cardinal ligaments in front of the cervix, or the lower portion of the uterus if the cervix has been amputated. The purpose of this is to place the lower pole of the uterus backward, to elevate and antevert the uterus, these three criteria being considered essential in the cure of uterine prolapse when the uterus is retained. This is similar to the principle advocated by Alexandroff,<sup>1</sup> in 1903, and Tweedy,<sup>10</sup> in 1905.

In 1933 W. Fletcher Shaw,<sup>9</sup> read a paper on the subject of the Manchester operation before the American Gynecological Society, which was published in the *American Journal of Obstetrics and Gynecology*. Following this publication, the Manchester operation was taken up by several gynecologists in America, and a number of papers have appeared on the subject since that time. It is excellent for the cure of prolapse, regardless of the size of the uterus. It is well adapted to the senile, atrophied uterus. The cervix may or may not be amputated according to the length and condition of this organ. The operation is necessarily completed by an adequate pelvic floor repair. Personally, I have used this method more and more during the last few years and in cases where formerly I would have performed the interposition operation. In my hands the results have been uniformly good, and at present I am inclined to choose it in preference to any other method when the uterus is to be conserved. There is practically no shock, it can be readily performed with a small dose of spinal anesthesia, which I prefer, or with local anesthesia, and it is well supported by old women who ordinarily would not be considered good surgical risks. Because of the growing interest in

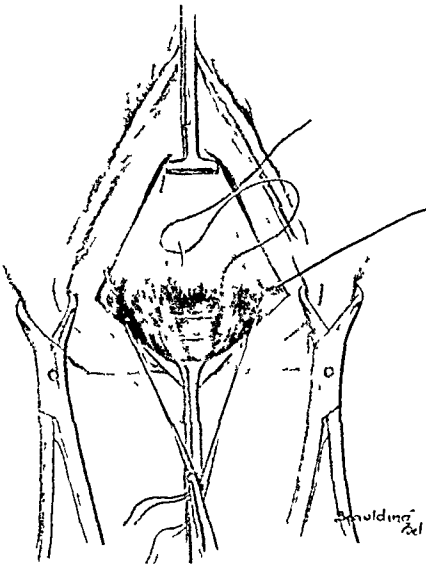


FIG. 9. The pelvic floor is opened at the mucocutaneous border the posterior vaginal wall is dissected from the rectum and the levator ani muscles and their fascia. The pelvic slings are approximated by three interrupted sutures of No. 1 chromic catgut.

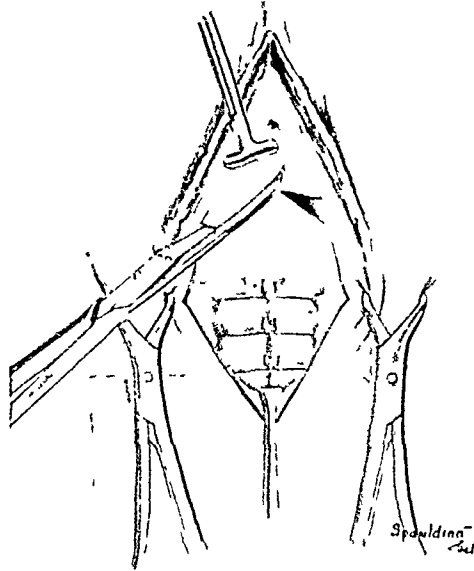


FIG. 10. The levator ani muscles and their fascia have been approximated by three interrupted sutures of No. 1 chromic catgut. The excess of the posterior vaginal wall is resected and the vagina is closed with interrupted sutures of No. 1 chromic catgut.

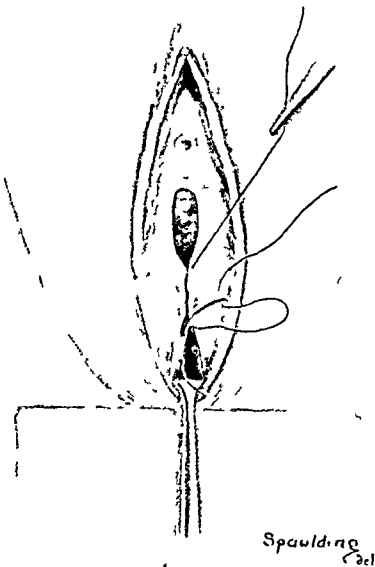


FIG. 11. Colles's fascia is approximated by a running suture of No. 0 chromic catgut.

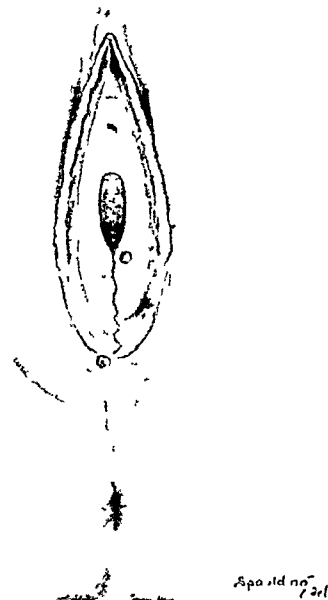


FIG. 12. The incision at the mucocutaneous border is closed by a subcuticular or a running suture of No. 0 chromic catgut, the ends of which are arrested by lead shots. In young women the vaginal introitus should be left larger.

this operation, the technique is described by illustrations accompanied by legends.

#### POSTERIOR VAGINAL HERNIA OR HERNIA OF THE CUL-DE-SAC OF DOUGLAS

Posterior vaginal hernia, also known as hernia of the cul-de-sac of Douglas and posterior vaginal enterocele, has received but scant attention up to recent years. In 1924, I<sup>7</sup> reviewed the literature of the subject and found but seventeen citations, the earliest mention being that of Marion<sup>5</sup> of Paris, in 1909. Formerly the lesion was confused with a rectocele. Patients were operated on for prolapse, and, if a hernia of the cul-de-sac was not discovered and repaired, there followed a mass which bulged over the recently repaired perineum as the patient assumed the upright position after operation.

In a paper read before the American Medical Association, published in 1922, George Gray Ward,<sup>11</sup> put this lesion on a sound basis and proposed a vaginal operation for its obliteration. Since the publication of Ward's paper, a few others have appeared in the literature. Ward's method consists of dissecting the posterior vaginal wall from the cul-de-sac of Douglas, removing the hernial sac, closing its base by sutures, approximating the uterosacral ligaments in the median line in order to obliterate the space into which the herniation had taken place, and building the perineum. The operation proposed by Marion,<sup>5</sup> is done through the abdomen and consists of superimposed purse-string sutures, obliterating the cul-de-sac of Douglas.

In 1912, Moschcowitz<sup>6</sup> proposed a similar operation in the treatment of prolapse of the rectum. His method, which is adequate for the purpose for which it was invented, is also extremely helpful in the management of cul-de-sac hernias. Most gynecologists prefer to treat these hernias through the vagina, by Ward's technique. However, occasionally one may encounter a very large hernia or a hernia complicated by adhesions, or one may discover such a

lesion during the course of a pelvic laparotomy, when the abdominal method of obliteration may be thought to be the better procedure. The overlooking of a hernia of the cul-de-sac of Douglas is responsible for most recurrences in the posterior vaginal segment, when an otherwise adequate operation has been done. The bladder and uterus will usually stay up, the perineum will give good support, but the large hernia, rolling over the well repaired perineum, will be responsible for the recurrence.

TABLE I  
PROLAPSE OPERATIONS\*

1. Vaginal plastics and uterine suspension or fixation	106
2. Interposition operation (Watkins-Schauta-Wertheim)	207
3. Vaginal hysterectomy (Mayo)	82
4. Vaginal hysterectomy (Price-Kennedy)	24
5. High vaginal fixation of the uterus	51
6. Colpectomy, subtotal, LeFort	23
Total	6
7. Interposition of cervical stump in inversion of the vagina following supravaginal hysterectomy	29
8. Manchester operation (Donald-Fothergill)	3
Total	50
Total	552

\* There were also 40 operations for cul-de-sac hernias

As shown by Table I, I have personally operated on 552 women for prolapse, and on forty for hernias of the cul-de-sac of Douglas. Individualization of patients has been attempted and eight different methods have been employed in the management of this group. There were seven deaths, five after the interposition operation, and two after vaginal hysterectomy (Mayo.) The causes of deaths after the interposition operation were cerebral hemorrhage, diabetic coma, cerebral embolism, acute cardiac dilatation, and pulmonary embolism. The causes of death after vaginal hysterectomy (Mayo) were uremia, ureters patent to catheterization in one woman, and uremia in a woman whose ureters had been angulated by attaching the united broad ligaments to the upper angle of the vaginal denudation. All these deaths occurred early in the series, a number of

years ago. My last statistical paper<sup>8</sup> was finished in December, 1935 and published in September, 1936. Since then there has been no mortality in 170 consecutive operations of all types. The gross mortality now stands at 1.2 per cent.

In my hands the recurrences have averaged between 8 and 10 per cent. As pointed out above, these are likely to be found if the patients are followed over a period of many years. The percentage of recurrences is decreasing as time goes on, probably because of better judgment in selecting the best operation for the individual patient.

#### CONCLUSIONS

1. Uterovaginal prolapse in young women, during the child-bearing age, may be satisfactorily treated by repairing the cervix, the anterior and posterior vaginal walls, and the perineum, by shortening the uterosacral ligaments and by performing a round ligament suspension of the uterus.

2. After the menopause the condition may be treated by vaginal plastics and fixation of the uterus, or by methods performed entirely through the vagina. Preference is usually given to the vaginal operations on account of lessened morbidity and mortality, and on account of increased operability. In my practice an abdominal incision is made in only a limited number of cases, to obliterate a very large posterior vaginal hernia.

3. The interposition operation, Watkins-Schauta-Wertheim, followed by an amputation of the cervix, gives excellent results in first and second degree prolapse and in cases of large cystocele. Vaginal hysterectomy, with interposition of the united broad ligaments (Mayo operation) is reserved for women with atrophied uteri, and when uterine or cervical pathology is present.

4. Vaginal hysterectomy (Price-Kennedy) clamp method, finds a definite place in the management of prolapse in old women and poor surgical risks, where the time element is an important factor.

5. High vaginal fixation of the uterus, with amputation of the cervix, is useful in the first and second degrees of prolapse, with a large cystocele, and when recurrence has occurred subsequent to an abdominal fixation of the uterus.

6. In worn out and feeble old women, where an extensive vaginal operation is contraindicated, subtotal colpectomy (LeFort operation), or total colpectomy (Dujarier and Larget operation), especially when performed under local anesthesia, may render great service.

7. One or the other method of colpectomy may be used to advantage in inversion of the vagina following supracervical or total hysterectomy.

8. In younger patients who have inversion of the vagina, including the cervical stump, following supravaginal hysterectomy, interposition of the cervical stump between the bladder and the vagina may correct the condition.

9. The Manchester or Donald-Fothergill operation is an excellent procedure in cases of first and second degree, or even third degree prolapse, regardless of the size of the uterus, whether normal in size or atrophied. The cervix is usually amputated in connection with this operation, when it is elongated, lacerated or irritated. The popularity of this method has increased considerably during the last few years.

10. An adequate repair of the pelvic floor is essential in all cases, with the rare exception of cases of nulliparous prolapse, where the perineum is intact and gives good support.

11. A hernia of the cul-de-sac of Douglas, posterior vaginal hernia, should be attended to in conjunction with the repair of the pelvic floor.

12. Local and spinal anesthesia may be used advantageously in a number of these patients.

13. A total of 552 personal cases of uterovaginal prolapse and forty cases of hernia of the cul-de-sac of Douglas is reported.



## REFERENCES

1. ALEXANDROFF, S. A. *Zentralbl. f. Gynäk.*, p. 27, 1903.
2. BAER, J. L., REIS, R. A., and LAEMLE, R. M. *Am. J. Obst. & Gynec.*, 34: 827, 1937.
3. DONALD, A. J. *Obst. & Gynaec., Brit. Emp.*, 28: 256, 1921.
4. EVERETT, H. S., *Surg., Gynec. & Obst.*, 61: 403, 1935.
5. MARION. *Rev. de gynéc. et de chir. Abdom.*, 13: 465, 1909.
6. MOSHCOWITZ, A. V. *Surg., Gynec. & Obst.*, 15: 7, 1912.
7. PHANEUF, L. E. *Am. J. Obst. & Gynec.*, 9: 507, 1925.
8. PHANEUF, L. E. *Surg., Gynec. & Obst.*, 63: 385, 1936.
9. SHAW, W. F. *Am. J. Obst. & Gynec.*, 26: 667, 1933.
10. TWEEDY, H. J. *Obst. & Gynaec., Brit. Emp.*, 12: 349, 1905.
11. WARD, G. G. *J. A. M. A.*, 79: 709, 1922.
12. WARD, G. G. *South. Surgeon*, 8: 307, 1939.
13. WATKINS, T. J. *Am. J. Obst. & Gynec.*, vol. 15, 1899.



CHANGES [in the menstrual flow] may indicate a great variety of pathologic states. Excessive flowing may be due to fibroid tumors of the uterus, mucous polyps, a benign hypertrophy of the mucosa or adenocarcinoma of the uterine body; or again, it may result from the incomprehensible disorder known as uterine insufficiency.

From—"A Textbook of Surgery" by John Homans (Thomas).

# LYMPHOGRANULOMA VENEREUM IN THE FEMALE

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**L**YMPHOGRANULOMA venereum now seems to be the acceptable name for a disease with so many appellations as to confuse even workers in the field of venereal disease. Four years ago we described some urethral lesions as "lymphopathia venereum,"<sup>1</sup> a term originated by Wolf and Sulzberger.<sup>2</sup> This seemed to be a superior term. However, since the Cumulative Index now lists this as lymphogranuloma venereum, the future literature should be correlated under this title. Among many other names this disease was called tropical or climatic bubo. The most widely known name in recent years has been lymphogranuloma inguinale. It was originally applied by Durand, Nicolas and Favre<sup>3</sup> in 1913 to chronic inguinal adenitis with multiple draining sinuses. The term was applied because of an apparent microscopic similarity with Hodgkin's disease ("lymphogranuloma").

The study of this condition progressed little or none until 1925, when Frei<sup>4</sup> discovered the diagnostic properties of an antigen prepared from the bacteriologically sterile pus removed from buboes. This important skin test gave impetus to world wide studies and a tremendous literature has developed. Many obscure lesions quite unconnected with the inguinal adenitis have now been brought together. The disease has been transferred to monkeys and to mice (Hellerström and Wassén,<sup>5</sup> and others), producing characteristic meningitis after intracerebral inoculation; to guinea pigs (Meyer, Rosenfeld and Anders<sup>6</sup>) producing a typical inguinal adenitis after inoculation in the groin; and to other animals. The filterable virus nature of the causative agent has been made clear by a number of investigators. It has been cultured on tissue-Tyrodé media by Tamura.<sup>7</sup>

The entity of this virus disease is undisputed at the present time.

## PATHOLOGY

*Gross Pathology.* By means of the antigenic test inguinal adenitis has been shown to be the least important manifestation of the disease in the female. Various ulcerations of the vulva and vagina, elephantiasis of the vulva, hypertrophic rectal tags, proctitis and rectal stricture may represent different forms of the same disease. Occasional cases with extragenital or generalized lesions have been described.<sup>8</sup>

The primary lesion is said to begin as a small superficial ulcer lasting for a few days to three weeks. We have interpreted as primary lesions the pinkish-red puffy urethral meatus and the superficial tender pinkish ulcer occurring most often in the fourchette or extending up one side of the vestibule. These lesions may heal and disappear after a few weeks, or they may extend more deeply into the tissues, forming chronic ulcers.

The secondary forms of this disease are usually explained by the characteristic extension of the inflammation along the lymphatics. If the primary lesion occurs on the upper two-thirds of the vulva, inguinal adenitis may follow because of the lymphatic drainage. Multiple small abscesses are formed in individual lymph nodes, accompanied by periadenitis and numerous burrowing sinus tracts which connect abscesses in various lymph nodes. As the process continues a progressively increasing purulent accumulation produces a tense abscess and the overlying skin may have the bluish appearance responsible for the term "blue balls." Intense pain may accompany this, apparently because of tension in the skin.

The abscesses may rupture and form multiple draining sinuses, which are extremely indolent in healing. Following heal-

In the early stages of involvement of the rectum, patients may have lassitude, low-grade fever, headache, slight deep pelvic

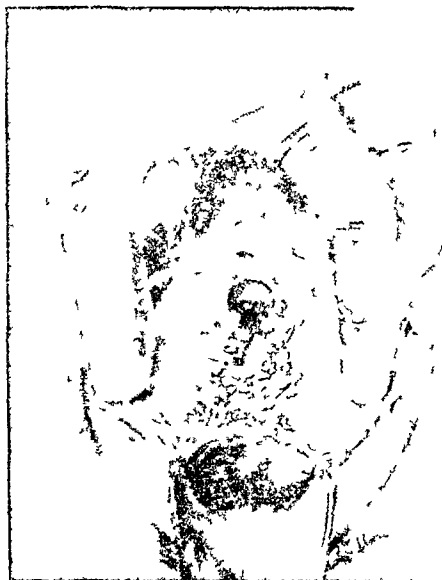


FIG 1 Lymphogranuloma venereum with ulcerative destruction of the anterior urethra.

ing there is scarring and puckering about the site of the bubo. The lymphatics may be blocked in the vulva with subsequent development of chronic edema with brawny skin and secondary ulcerations. This disease explains the majority of cases of "chronic hypertrophic vulvitis."

If the urethra is involved, there may be only a progressive ulcerative destruction up to the internal sphincter. This feature of the disease was described by Gray in detail in 1936.<sup>1</sup> We have never seen a vesicovaginal fistula or involvement of the cervix.

Since most ulcers occur on the inferior third of the vulva or on the posterior portion of the vagina, the inguinal glands are not so frequently involved in women as in men, where the lymphatics of the penis and scrotum drain to the inguinal glands. In the female all variations of ulcerations may appear about the vulva and vaginal orifice. Drainage from the lower vulva and vagina extends along the rectum. The rich bed of lymphatics about the ampulla may be extensively involved in a marked lymphangitis.



FIG 2 Elephantiasis of the labia major and clitoris with ulcerative destruction of the urethra.

pain and heaviness in the rectum. In such early cases there may be only tenderness on rectal examination. It seems that these might be suspected and a presumptive diagnosis made by the Frei test. If early treatment were instituted as suggested below, the late disastrous results might be averted. Apparently the infection penetrates the wall of the rectum to cause an ulcerative inflammation of the mucosa. The process may remain limited to the ampulla or extend far up the colon. These patients may lose weight, develop secondary anemia and suffer much pain accompanied by mucopurulent discharge. In later stages there is a marked scarring with contraction which produces the typical corrugated rectal stricture. The disease may extend by the lymphatics to the anus with the production of typical large elongated anal tags. The interesting recent work of Paulsen,<sup>9</sup> using bowel discharge and bowel tissue antigens, corroborates the identity of this form of lymphogranuloma venereum.

Whether the condition can involve the uterus and tubes is quite unsettled. The pathologic diagnosis in the Fallopian tube

is very questionable. Not infrequently the patient with rectal ulcerations and stricture may have broad ligament induration or

scesses. Marked scarring of the capsule and infiltration with plasma cells follow. Many authors mention giant cells that are



FIG. 3. Elephantiasis vulvae with complete ulceration of the vestibule in a 22 year old negress. The urethra opens in the depth of the ulceration and hypertrophic tags surround the vaginal orifice.

pelvic abscess. These complications seem more likely due to extension from the rectum than to primary involvement of the upper genital tract. Cases with bacteriologically sterile pyosalpinx should be studied by animal inoculation and for antigenic effects.

*Microscopic Pathology.* A review of the pathologic studies indicates that the most characteristic microscopic findings are present in the acute or subacute inguinal bubo. D'Aunoy and von Haam<sup>10</sup> describe a proliferation of the endothelial cells lining the lymph spaces of the glands. Masses of large epithelial cells occur in more or less circumscribed nodules. Central necrosis with leucocytic infiltration may form characteristic triangular or quadrangular ab-

common and resemble either Langhans or Reed-Sternberg cells. According to D'Aunoy and von Haam, no characteristic lesions can be noted in chronic conditions.

Pund, Greenblatt and Huie<sup>11</sup> are very enthusiastic over the value of biopsy for the diagnosis of various venereal diseases, having determined as many as three different venereal diseases in one lesion. If this is confirmed a remarkable advance will have been made. A majority of investigators do not agree that microscopic diagnosis is as accurate as suggested by Pund and his co-workers.

In the chronic lesions there is a progressive lymphangitis frequently accompanied by chronic edema and sclerosing fibrosis of the subcutaneous and submucous tissues

resulting in enlargement and induration of the affected parts. Insufficient circulation may cause ulceration.

Edwards and Kindell<sup>12</sup> give an excellent description of the pathology in rectal stricture. The polypoid internal surface is made up of vascular granulation tissue infiltrated by a variety of cells. The submucosa is thickened and fibrous. Inflammatory infiltration and scarring extend throughout the muscular coats and into the fat. The accumulation of lymphoid and plasma cells is massive; in the outer coats, perivascular. Eosinophiles are scattered throughout. There are many mononuclear wandering cells. Many small abscesses or sinus tracts may contain bits of fecal material and foreign bodies with definite foreign body giant cells. Small, nodular, tubercle-like structures made up of epithelioid cells, in some containing giant cells of the Langhans type, are present in almost every specimen.

D'Aunoy and Schenken<sup>13</sup> found in a Fallopian tube numerous stellate abscesses surrounded by typical masses of endothelial cells from a patient with a positive Frei test. While this may be suggestive, it does not prove that lymphogranuloma venereum causes salpingitis.

We are forced to conclude that fairly characteristic but probably not diagnostic lesions occur in subacute inguinal adenitis. Other lesions are not nearly so characteristic. This is perhaps due to the marked secondary infection in the ulcerative lesions. The greatest single value of biopsy is to rule out malignancy.

A few authors have felt that these ulcerative lesions may be premalignant. Pund, Greenblatt and Huie<sup>11</sup> described three cases with development of epitheliomas in ulcers diagnosed pathologically as being of venereal origin. They thought there might be some causal relationship. David and Loring<sup>14</sup> presented two cases of long standing rectal strictures with subsequent development of squamous cell carcinomas at the site. In our experience we have never seen a case with cancer

developing in lymphogranuloma venereum and believe there is no increased occurrence of malignancies due to the disease. Microscopic sections of old lesions may show marked proliferation of squamous epithelium and endothelium from the capillaries, superficially suggesting malignancy. Biopsies should be taken from all cases with chronic ulcerations, as even the experienced individual can be mistaken in a gross diagnosis.

#### OCCURRENCE

In recent months we have performed 326 routine intradermal Frei tests on patients at the Louisville City Hospital. Of these 127 tests were done on obstetrical patients, white and colored, and the remainder on white and colored, male and female patients on the medical and surgical wards. Our criterion for a positive reaction has been that most commonly accepted, i.e., a definite nodule measuring at least 5 mm. in diameter. The tests were read within forty-eight to seventy-two hours of their administration. In this series, twenty-seven patients (8.3 per cent) were found who had a definitely positive reaction to the Frei antigen.

Of sixty-eight tests performed on white obstetrical patients, not one was found who had a positive Frei reaction, while in fifty-nine colored obstetrical patients, only three reacted to the antigen. Conversely, in thirty-eight tests on white women admitted on the gynecologic service, four were positive, and in forty-five tests on colored patients admitted on the same service, seven were positive. This would seem to raise the question as to whether the lymphogranuloma venereum does produce some degree of sterility or whether the type of patient ordinarily seen suffering with lymphogranuloma venereum is the sexual derelict prone to all the diseases of the reproductive system and not given to child-bearing.

In a series of 183 routine Frei tests on colored gynecologic patients previously done by one of us (L. A. G.) at the Johns

Hopkins Hospital in Baltimore, forty-one (22.4 per cent) were found who reacted positively to the antigen. Comparing these results with those obtained on a similar group at the Louisville City Hospital, where 15.5 per cent positives were found in forty-five colored gynecologic patients, it would seem that the history of the disease is substantiated; that is, that the progress of the disease is from the seacoast inland, and that the incidence in Louisville may for this reason not be as great as it is in Baltimore.

Of the twenty-seven Louisville patients reacting positively to the antigen, twenty-one gave a history compatible with the infection and six denied knowledge of ever having experienced any evidences of the disease. The interval of time that had elapsed between performance of the test and the date of the disease as given by the patient varied from a few weeks to twenty-nine years. Dmeltcos and Ducrey tests were performed at the same time as the Frei test, and in each case of a positive history either the test for lymphogranuloma venereum or for chancroid was positive. Of the forty-one who gave positive reactions to the Frei antigen in Baltimore, twenty-six gave positive histories while in fifteen there was no definite history to indicate existence of the infection.

It is extremely important to bear in mind when using the Frei or allied skin tests, that all but a very small percentage remain positive for life unless the patient has been desensitized. Occasional cases with negative tests may be due to anergy or lack of allergy. It also seems likely that the tests will not produce a positive reaction until an interval of two or three weeks after the infection. The Frei test would appear indispensable in the diagnosis of patients with venereal disease. The interpretation of results must be carefully integrated with a complete understanding of the clinical manifestations of the disease and the reading of the test.

The present methods of securing and preparing the antigen makes it impractica-

ble for the use of the individual practitioner, but certainly no gynecologic or venereal clinic should be without it. Refinements that are being made in the mouse brain antigen (removal of the factor of sensitivity to the mouse brain itself) seem likely to make a reliable commercial product available in the not too distant future.

#### TREATMENT

The methods of treatment of lymphogranuloma venereum have been so many and varied as to suggest immediately that none of them are of any great value, but recently we have been given reason to hope for better results.\*

The use of Frei antigen as treatment, in our hands, has seemed to be efficacious. We have experimented rather widely with its use both intradermally and subcutaneously. Of the two methods, the intradermal route is distinctly the method of choice. Using intradermal injections, two, or preferably three times a week, one may expect a subsidence of the majority of lymphogranuloma venereum buboes that are not well along toward suppuration, within two to three weeks. Patients with rectal stricture complaining of great amounts of rectal discharge (sufficient to necessitate the constant wearing of pads), have invariably volunteered the same information, i.e., within a few days after being started on the treatment their discharge has increased very perceptibly in amount, but become quite thin in character. After a period of ten days there has been a noticeable checking of the flow until within a month all who continued on the regimen were able to discard the pads. They further have reported loss of sensation of heaviness in the rectum and an increased feeling of well-being. Many patients who previously had been subjects for repeated manual

\* This work has been done in the Genital Lesion Clinic of the Louisville City Hospital under the direction of one of us (M. L. B.) and in close coöperation with the Departments of Dermatology and Bacteriology. A more detailed report will be made in the near future.

dilatations of the rectum at ever diminishing intervals, have found that the intervals were considerably lengthened while on treatment.

The use of the antigen as treatment has given good results with the primary chancre of lymphogranuloma venereum occurring in the vaginal fourchette. Of three cases with persistent lesions of the female urethra, two were completely cleared up with the use of the antigen. The third was resistant to all therapy, including sulfanilamide, but improved remarkably following prolonged administration of antigen.

Recently sulfanilamide has been introduced for the treatment of lymphogranuloma venereum. This drug seems to hold considerable promise for therapy of this condition. To date we have had only six cases of buboes progress to suppuration during the course of the administration of this drug. On questioning, four of these patients have frankly admitted failure to keep up an adequate dosage of the drug. The use of sulfanilamide seems to be of benefit to the patient with rectal stricture or those with a persistent primary. Whether its action is on the virus or on the secondary pyogenic invaders, as suggested by Torpin, Greenblatt, Pund, and Sanderson,<sup>15</sup> we are unable to say. Results from the use of this drug in the treatment of lymphogranuloma venereum are certainly far short of its rather miraculous effect in the therapy of chancroidal lesions and chancroidal buboes. In the treatment of lymphogranuloma venereum buboes, the swelling and pain are reduced considerably within a few days, but in our experience one may expect an interval of several weeks for the complete subsidence of enlargement of the glands. One feature has struck us rather forcibly. Whereas previously in this institution fluctuant lymphogranuloma venereum buboes were quite prevalent, in recent months they have become almost a rarity. In reviewing this incidence we find that it coincides almost precisely with the date when sulfanilamide first attained its very widespread use, both in our clinics

and by private physicians, in the treatment of gonorrhea and other diseases.

We do not know how long a patient may retain the ability of infecting others or in just what stage the disease must be in order for the infection to be transmitted. It seems to us theoretically possible that the general use of the drug is either eliminating many of the sources of infection or is serving as a prophylactic agent while being used as therapy for other conditions.

In the treatment of chronic hypertrophic vulvitis, vulvectomy should be performed only when the suture line joining the vestibule is free of ulceration. Otherwise it is likely to separate widely with the formation of an encircling ulceration slow to heal and prone to severe hemorrhage early after operation. The results are most gratifying where the suture line is clean.

In many cases with stricture of the rectum and marked ulceration with bleeding and discharge, sigmoidostomy is followed by general improvement and abatement of the local symptoms. Occasionally the inflammatory process may ascend to the colostomy opening, causing stricture and necessitating additional higher colostomies. In these cases, however, there is usually some involvement at the time of operation in the original colostomy. Warthen<sup>16</sup> has suggested an operation by which the lower pelvis is closed off from the upper abdomen by peritoneal sutures before the colostomy is performed. Subsequent dilatation of the rectum is thought to be less dangerous in producing generalized peritonitis. Edwards and Kendall<sup>12</sup> have had good results in excising the rectum by the Lockhart-Mummery method.

#### SUMMARY AND CONCLUSIONS

Lymphogranuloma venereum is a well proved virus disease entity. Further variations in this disease will undoubtedly be found. The new concepts developed within the past fifteen years have gone far to clear up the confusion of many lesions in the female. One phase of diagnosis and treat-

ment should command the attention of every practitioner, namely: the zealous attempt to recognize and treat the early stage of rectal stricture. We believe that the acute involvement of the glands of Gerote must be accompanied by a fairly definite group of symptoms which may lead to a diagnosis substantiated by the Frei test. Intense treatment by Frei antigen, sulfanilamide or a combination of the two, may avert the eventual addition of another semi-invalid to a group already too frequently seen, particularly in the southern Negro female.

## REFERENCES

1. GRAY, L. A. Lymphopathia venereum; "lymphogranuloma inguinale" of the female urethra. *Surg., Gynec., & Obst.*, 62: 745, 1936.
2. WOLF, J., and SULZBERGER, M. B. Lymphopathia venereum (Lymphogranulomatosis inguinalis) and the Frei test. *Brit. J. Dermat.*, 44: 192, 1932.
3. DURAND, J., NICOLAS, and FAVRE. Lymphogranulomatose inguinale subaigue d'origine genitale probable, peut-être venerienne. *Bull. et mem. Soc. med. d. hôp. de Paris*, 35: 274, 1913.
4. FREI, W. Eine neue Hautreaktion bei "Lymphogranuloma inguinale." *Klin. Wchnschr.*, 4: 2148, 1925.
5. HELLERSTRÖM, S., and WASSÉN, E. Meningo-enzephalitische Veraenderungen bei Affen nach intracerebraler Impfung mit Lymphogranuloma inguinale. *Cong. Internat. de Dermat. et Syphilol.*, p. 1147, 1930.
6. MEYER, K., ROSENFELD, H., and ANDERS, H. E. Erfolgreiche Uebertragung des Lymphogranuloma inguinale auf Meerschweinchen. *Klin. Wchnschr.*, 10: 1653, 1931.
7. TAMURA, J. T. Virus of lymphogranuloma inguinale. *Northwest Med.*, 36: 39, 1937.
8. EBERHARD, T. P. Generalized lymphogranuloma inguinale. *Ann. Surg.*, 107: 380, 1938.
9. PAULSON, M. Diagnosis of colitis associated with virus of lymphogranuloma venereum by bowel antigen. *Am. J. Digest. Dis.*, 5: 554, 1938.
10. D'AUNOY, R., and VON HAAM, E. Venereal lymphogranuloma. *Arch. Path.*, 27: 1032, 1939.
11. PUND, E. R., GREENBLATT, R. B., and HUIE, G. B. Role of biopsy in diagnosis of venereal diseases. *Am. J. Syph. & Neurol.*, 22: 495, 1938.
12. EDWARDS, M., and KINDELL, F. B. Treatment of rectal lymphogranuloma by excision. *Surgery*, 4: 800, 1938.
13. D'AUNOY, R., and SCHENKEN, J. R. Lymphogranuloma as a cause of pelvic inflammatory disease. *J. A. M. A.*, 110: 799, 1938.
14. DAVID, V. C., and LORING, M. Relation of chronic inflammation and especially lymphogranuloma inguinale to the development of squamous cell carcinoma of the rectum. *Ann. Surg.*, 109: 837, 1939.
15. TORPIN, R., GREENBLATT, R. B., PUND, E. R., and SANDERSON, E. S. Lymphogranuloma venereum in the female. *Am. J. Surg.*, 43: 688, 1939.
16. WARTHEN, H. J. Treatment of benign rectal strictures (lymphogranuloma venereum). *Virginia M. Monthly*, 66: 20, 1939.





# VAGINAL HYSTERECTOMY—ITS INDICATIONS AND TECHNIQUE\*

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VAGINAL hysterectomy is not a new procedure. Our grandfathers in gynecology, the founders of our special societies, were thoroughly familiar with its technique and indications. When, however, "perityphlitis" was found to be appendicitis and operation promised much in its cure, then the surgeons began to invade the abdomen for "chronic" appendicitis. While inside they discovered Jackson's membrane, cecum mobile, and a number of other anatomic deviations, and placed much stress upon their correction. Then gynecologists became enthused over this new surgery and departed from their vaginal technique in order to combine their indicated pelvic work with these new operative wrinkles. In consequence, vaginal surgery became neglected and recently one could find busy clinics where not a single vaginal hysterectomy had ever been performed either by the present staff or by their predecessors. Since the prophylactic surgery described above is known now to be meddlesome and frequently harmful and since the vaginal approach to pelvic disease is associated with less mortality, a smaller morbidity rate and a much more rapid convalescence, it is high time that present day gynecologists learned to appreciate the value of vaginal hysterectomy, acquire its technique, and extended its use.

In vaginal surgery, because of the restricted field, more delicate instruments are necessary than in abdominal work. A retractor a little too wide may make difficult an otherwise easy operation. The operating table should be such that when the patient is in the lithotomy position the pelvis is in the proper plane, tipped neither

too far upward or backward. A good spotlight thoroughly to illuminate the operative field is indispensable.

The beginner in vaginal surgery would do well to select his first cases for vaginal hysterectomy with considerable care, picking out easy cases until, as his skill increases, he may elect to do more difficult ones. The vagina should be roomy enough to allow the necessary manipulations. A narrow introitus can be overcome by a small episiotomy incision. A vaginal vault which is poorly developed or constricted will cause great difficulty. On the other hand, it may be easier to operate upon a nullipara than upon a multipara with too roomy a vagina, where the walls may fall together laterally and obscure visibility.

The uterus should not be too big. The first cases should allow the uterus to be delivered intact so as to allow prompt recognition of its upper attachments. When more experience has been obtained a uterus a little too large may be divested of its cervix to allow its removal. Later when one has learned to recognize the round ligaments and the attachments of the tubes and ovaries under all conditions, tumors of large size may be tackled for morcellation. The larger the tumor, however, the greater the chance of running into unexpected pathology in the appendages or the uterus itself.

The uterus should be freely movable. Fixation may be due to previous pelvic infection, so that the uterus may be surrounded by adhesions, and the appendages may be fixed and inaccessible, or it may be due to malignancy and the uterus be irremovable. A vaginal hysterectomy may

\* From the Obstetrical and Gynecological Departments, Rush Medical College, University of Chicago, and Presbyterian Hospital.

be safely done in spite of this contraindication but it may call for much dexterity and caution on the part of the operator.

The operation should not be attempted if the patient has had previous pelvic surgery, especially by laparotomy. Adhesions of the intestine to the uterine body or appendages commonly form even after attention by experts. If these are encountered, sharp dissection with care to leave a bit of the uterine tissue on the intestine instead of the reverse, is usually easy, though one must be prepared to suture quite promptly any injury made to the intestine. Before transgressing this contraindication, one should rule out by careful history-taking, the probability of a previous intestinal obstruction, because there may be loops of intestine adherent to the old abdominal incision which cannot be loosened by the vaginal route, and which may precipitate an obstruction during convalescence due to overdilatation of the guts. Particular attention should be paid as to whether there has been a previous uterine fixation or such an operation as might result in fixation. If this is encountered anyway, careful boldness may solve the difficulty. One should not work blindly; if reasonable headway is not made, then the cervix should be cut off, bleeding points sutured, a large pack introduced into the pelvis to press against the uterine body, the vaginal vault closed carefully, the abdomen opened and the operation completed. I have had to desert the vaginal route and proceed abdominally only twice and in both instances the necessity arose because of a previous fixation of the uterus. In either case was the recovery any different than would be expected after the usual laparotomy.

If vaginal hysterectomy has been decided upon, the patient, after the usual preparations, is anesthetized with ethylene gas and when asleep is placed in the lithotomy position. After thorough cleansing of the vagina and vulva with soap and water, the vagina is well but gently swabbed with

Lugol's solution and the bladder emptied by the use of a catheter.

The cervix is grasped with a bullet forceps and pulled down as far as possible. If, in spite of previous cauterizations, the cervix does not seem free of infection it is thoroughly cauterized again at this time. An injection of 2 c.c. of obstetrical pituitary extract is given into the paracervical tissue so as to make the operation as bloodless as possible. A transverse incision is made through the mucosa anteriorly, below the attachment of the bladder. If there is doubt as to how low the bladder lies on the front of the uterus a sound may be introduced into the bladder to determine this point. The anterior wall of the vagina with the attached bladder is then separated from the anterior wall of the uterus. Sometimes this proceeds easily by use of the gloved finger or with gauze, but frequently sharp dissection is necessary. At any rate, one must keep rather towards the uterus than towards the bladder. If, in spite of care, the bladder is unavoidably entered, the mucosa should be sutured with interrupted No. 0 chromic catgut and the muscularis similarly sutured over the mucosal row. After the operation a retention catheter is placed in the bladder, to be removed when the patient is allowed out of bed. If the plica vesicouterina is easily found, it is incised and a narrow bladed retractor inserted into the peritoneal cavity. If an anterior repair is to be made or a prolapse corrected, before the peritoneum is opened, the bladder is freed from its attachments to the anterior vaginal wall up to the anterior urinary meatus. If a prolapse is being operated upon or if urinary incontinence exists, the entire length of the urethra is exposed and the fascia lying to each side of it is brought together over the urethra with two or three No. 1 chromic catgut sutures. The vaginal mucosa is then closed with the same sutures over the urethra. The removal of the excess vaginal mucosa and the completion of the anterior repair is postponed until the uterus has been removed.

If the plica vesicouterina is not promptly found the search is abandoned and an approach to the posterior cul-de-sac is started. A transverse incision is made through the mucosa posterior to the cervix at the height of the posterior vaginal fornix. The mucosa is pushed backwards to expose the peritoneum which is incised and a narrow bladed retractor is inserted there. Occasionally the posterior cul-de-sac is also not easy to enter. Instead of wasting time and unduly traumatizing the tissues, one then proceeds to the loosening of the uterus from its attachments. The anterior and posterior vaginal mucosa incisions are united by a lateral incision on each side of the cervix and the mucosa pushed back about  $\frac{1}{8}$  inch on each side. Whether the peritoneum has been entered or not, the sacrouterine ligaments are now clearly exposed. The left sacrouterine ligament is firmly clamped with a slender curved clamp, the ligament cut on the uterine side and the clamp replaced by a No. 2 chromic catgut fixation ligature, which suture material is used throughout the rest of the operation. In the same way the exposed portion of the lower end of the broad ligament immediately above the sacrouterine ligament is similarly clamped divided and ligatured. If one was successful in entering both the anterior and posterior cul-de-sacs as in the uncomplicated technique, then if both retractors are held strongly apart and to the left side, the uterine vessels can now be seen, clamped and ligated without fear of interfering with the ureters. If neither cul-de-sac has been entered, as soon as the left sacrouterine ligament has been clamped, incised, and ligated, the right sacrouterine ligament should be similarly disposed of. Severing both sacrouterine ligaments allows the uterus to be pulled further down. If not previously possible, the posterior and anterior cul-de-sacs should now be possible of entry. When both uterine vessels have been clamped and loosened the uterus can be still further drawn out. Ordinarily at this stage, the body of the uterus presents at the posterior

opening and by the use of bullet forceps can be delivered into the vagina, the fundus down. The upper part of the broad ligament is clamped and disposed of, as was done with the lower portions of the broad ligament, except where the sacrouterines were left with a double strand of catgut to identify them; the upper portions are left with a long single strand attached. The first clamping of the upper end of the broad ligament usually includes the suspensory ligament of the ovary, the uterine end of the Fallopian tube and the round ligament. The rest of the broad ligament is freed by clamps and fixation sutures, and the opposite side is then similarly attended.

When the uterus is somewhat too large for delivery intact, the cervix may be cut off just below the ligated uterine arteries, which reduction in size usually allows easy delivery of the uterine body. If the remaining mass is still too large, as much as possible is to be excised, either by a long handled scalpel or sharp scissors, in a succession of morcellations until the entire uterus can be delivered. This should be done under full vision, and before each chunk is removed the remaining portion should be fixed in position with a bullet forceps to prevent retraction and to control bleeding. As early as possible during a morcellation the upper portion of the broad ligaments should be identified, clamped, and tied off, for with both uterine vessels already tied off there need be no fear of excessive bleeding after the ovarian vessels are securely ligated.

The appendages are now to be inspected. Pull down on each of the single stranded ligatures until the knot is visible, then seize the stump with a long Allis forceps and bring down the appendages and inspect for possible pathology. Occasionally pathology is encountered which is difficult of removal, in particular, adherent inflammatory adnexa. Such appendages can be loosened by gentle manipulation with the fingers, just as is done in abdominal operation. If the uterus has not been easily removed, especially if pedunculated fibroids were present, and particularly if morcella-

tion was necessary, then after the appendages have been disposed of, all instruments should be removed from the operative field and two fingers inserted through the vaginal vault to feel for possible uterine remnants since a pedunculated fibroid may have been peeled off the uterine body and left behind. Unless an intraligamentous nodule has been left such nodules are easily removed; if intraligamentous, more exactness is required.

All ligatures should now be inspected and hemostasis perfected. The pelvis is now ready for closure. If an anterior repair is to be done, the anterior vaginal flaps are excised and any spurs found are isolated and separately ligated instead of depending upon a running suture. If the patient had a prolapse the round ligaments are caught, each with a long Allis forceps as high up as possible. A chromic or silk suture is passed through the vaginal mucosa to the left of the vaginal flap just below the last suture used in covering the urethra after the urethroplasty. It is passed through the mucosa and a good bite of the lateral vaginal fascia is included; then it is passed around the round ligament as high up as possible on the left, and a similar bite is taken through the right round ligament. The suture then passes through the right vaginal fascia close below the internal urinary meatus and out through the mucosa close to the median incision. This suture is then carefully but firmly tied. This step anchors the round ligaments under the urethra and brings the bladder to rest upon the broad ligaments. When this is done, a couple of interrupted sutures will unite the broad ligaments together in the midline. If silk is used for the anchoring of the round ligaments its removal must be delayed until three or four weeks after the operation. Whether a prolapse operation is being performed or the patient is to have an anterior repair completed, interrupted sutures close the incision from the urethral area up to the vaginal vault.

The vaginal vault is then closed. A small pack is inserted to keep the intestines back.

A suture is passed through the right edge of the anterior vaginal cuff which takes several superficial bites of the denuded surface of the bladder and then picks up the anterior fold of the peritoneum. The ligature holding the upper portion of the broad ligament is drawn down, to expose the peritoneal fold running from the bladder to the broad ligament. The suture takes bites of the peritoneum until it reaches the broad ligament, where it is passed around the tubo-ovarian stump in order doubly to ligate the ovarian vessels. The suture now picks up the peritoneum of the broad ligament in successive bites until it reaches the stump of the uterine vessels and sacrouterine ligament, around each of which it is passed that these areas may be ligated again. The suture is passed through the right edge of the posterior peritoneal flap, through the vaginal wall and out into the right side of the posterior vaginal fornix. This suture, when tied, has anchored the broad and sacrouterine ligaments to the vaginal vault, doubly ligated the ovarian and uterine vessels, has performed a peritoneal toilet and has closed the right side of the vaginal vault. The left side is now similarly treated. Before tying this suture, if a deep cul-de-sac is present or if a prolapse is being treated, a suture is taken which ties both sacrouterines together and obliterates the cul-de-sac. The rest of the vaginal vault is closed with two or three interrupted sutures.

A posterior colpoperineorrhaphy is done if indicated. If the bladder has been injured, a urethroplastic operation is performed, or, if an extensive anterior repair has been done, then a hollow tip Mallencot two-wing rubber retention catheter is inserted into the bladder to be left there until the patient sits up. When the time comes for its removal the catheter is cut close to the urethra, the edge of the catheter is held by an artery forceps and a sound pressed into the catheter to lengthen the head, so that it may be withdrawn without dilating the urethral wall. After an ordinary hysterectomy the bladder is

emptied by a glass catheter and a vaginal pack is inserted to support the vaginal vault during coughing or vomiting. This pack is removed after twenty-four hours. The same attention is given the bladder as after abdominal hysterectomy.

On the seventh postoperative day perineal sutures, if present, are removed and the patient is allowed out of bed. The average length of stay in the hospital is twelve days.

This operation can be performed with a mortality of  $\frac{1}{3}$  per cent in a series of several hundreds of cases, not excluding

any as poor surgical risks but including delicate old women, a considerable portion of morcellations as well as nulliparae and virgins with intact hymens. The technique is not difficult. Anyone who can do an interposition operation nicely should have no particular difficulty in doing a vaginal hysterectomy well. A skillful gynecologist should be expected to perform every operation in his very restricted field. No operation, under certain conditions, can be more strictly indicated than a vaginal hysterectomy and frequently no other operation can be fairly substituted for it.



SINCE the various genital organs have a very limited number of responses to disease, any one symptom may represent a considerable number of pathological states, some of them very dangerous and others relatively harmless.

From—"A Textbook of Surgery" by John Homans (Thomas).

# CAUSES OF POSTMENOPAUSAL BLEEDING\*

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THE development of modern gynecology may be divided into three eras.

In the first, the pioneers ventured into and made great progress in operative technique. Those early surgeons soon brought to light an abundance of pathologic material which was carefully studied in the laboratories of the better clinics and thus a new era of cellular pathology, as applied to gynecology, was developed. The pathologists did much toward explaining the causes of uterine bleeding, but there were many cases in which both gross and microscopic studies of the tissues failed to explain adequately the bleeding.

While the development of operative technique and pathology was in progress some attempts were being made to understand the physiology of the sex organs. Some of this early work, such as that of Fraenkel, on the function of the corpus luteum, was of fundamental importance and has been amply substantiated by later workers. But most of our knowledge of sex physiology has developed from the work of the past fifteen years. This newer knowledge of physiology marks the third era in the development of gynecology. It is natural that gynecologists should attempt to utilize this knowledge to understand those cases of bleeding which were not satisfactorily explained on the basis of organic pathology. These attempts have given us some incomplete understanding of functional uterine bleeding. During and before the menopausal years this group is a large and important one but after the menopause an organic lesion can be found in almost all cases of bleeding. This is not to say that physiology has no place in the consideration of postmenopausal bleeding, for it has an important bearing in many cases. Nevertheless, even in those cases in

which there is an important physiologic factor an organic lesion is usually demonstrable as the actual cause of bleeding.

Some years ago we made a clinical and pathologic study of the causes of bleeding after the menopause. We studied the pathologic material and clinical cases occurring in the Johns Hopkins Hospital between January 1, 1919 and January 1, 1935. Our findings have been a constant reminder to us that the appearance of blood from the genital tract after the cessation of the menstrual life is a symptom which should never be considered lightly. A complete examination to locate the lesion responsible for the bleeding should never be deferred, for our findings indicate that the lesion responsible for the bleeding is usually a serious one and delay in treatment may take away from the patient her only chance of cure.

The most frequent lesion which we encountered was cancer of the cervix which occurred in 32.4 per cent of the cases. Cancer of the body of the uterus occurred in 14.9 per cent. The combined incidence of the two types of cancer of the uterus was 47.3 per cent. This figure, however, does not represent the total incidence of malignancy in the generative tract causing bleeding after the menopause. To it must be added the following: 3.1 per cent, representing the cases of malignant ovarian tumor; 1.4 per cent, representing cases of sarcomatous change in myomata; 0.9 per cent, representing the cases of sarcoma of the endometrium; 0.3 per cent, representing one case of sarcoma of the vagina; and 0.3 per cent, representing a case of carcinoma of the vagina secondary to carcinoma of the rectum. The total incidence of malignancy in our cases of bleeding from the vagina after the menopause is thus

\* From the Gynecological Department, Johns Hopkins University.

brought up to 53.3 per cent. (Fig. 1.) Our figures are in keeping with those found generally in the literature, the incidence of

with an excellent chance of cure if the lesion is detected reasonably early.

Since malignancy was responsible for

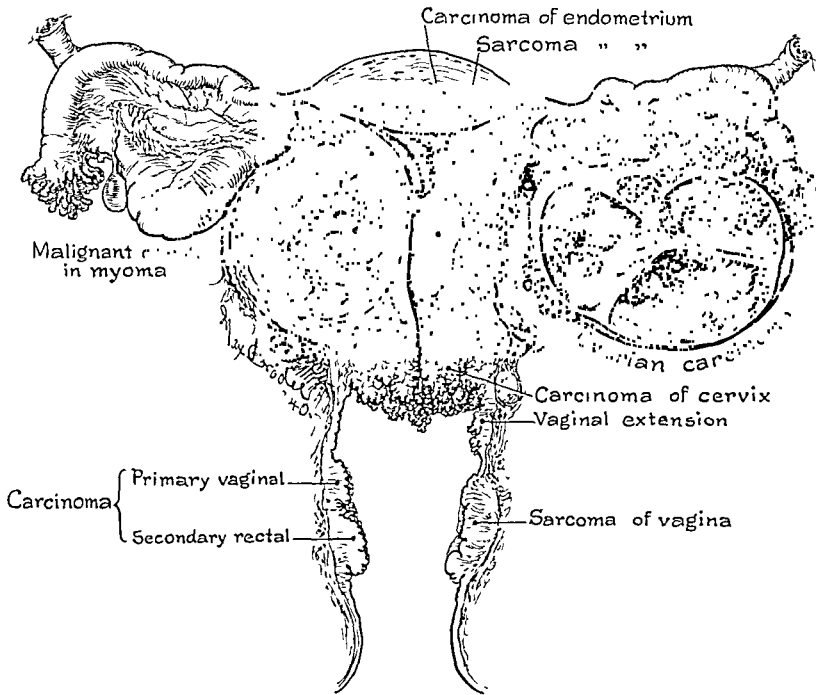


FIG. 1. Diagrammatic chart illustrating malignant causes of postmenopausal bleeding.

malignancy in most series being in the neighborhood of 50 per cent and in a few series considerably higher.

Stated as simply as possible, this means that a woman presenting herself with bleeding after the menopause has a greater than even chance of having malignancy. If the profession at large could be made to realize this single fact more women would be brought to treatment relatively early and many more cures could be effected. This is particularly true of the group with carcinoma of the body of the uterus. With cancer of the cervix, bleeding may occur early but all too often a rather extensive intracervical lesion is present before there is sufficient bleeding to attract the woman's attention. Fortunately, with cancer of the endometrium the growth begins in the delicate endometrial tissue which bleeds easily. Then, too, endometrial cancer starts in the center of a relatively free lying organ which can easily be removed

bleeding in 53.3 per cent of the cases, there remained a large group of cases (46.7 per cent) in which a benign lesion accounted for the bleeding. (Fig. 2.) Cervical ulceration due to prolapse accounted for the bleeding in 10.7 per cent of the cases. This lesion is obvious on inspection and its benign nature is usually apparent. If any doubt exists biopsy should be done if one contemplates an operation for the prolapse such as the interposition or Manchester operation in which the corpus of the uterus is to be saved. A curettage should also precede these operations to exclude, with certainty, a malignancy higher in the uterus.

In a considerable group of cases of slight bleeding after the menopause, postmenopausal vaginitis is responsible for the symptom. In our group the incidence was only 6.9 per cent, but the cases which we studied were all hospital admissions. In the majority of cases of vaginitis the lesion is obvious on speculum examination and the

cases are treated in the dispensary or physician's office. Hence, this small percentage is not a true index of the incidence

sexual intercourse is rare, adhesions form between the abraded, collapsed vaginal walls. The rupture of these adhesions at

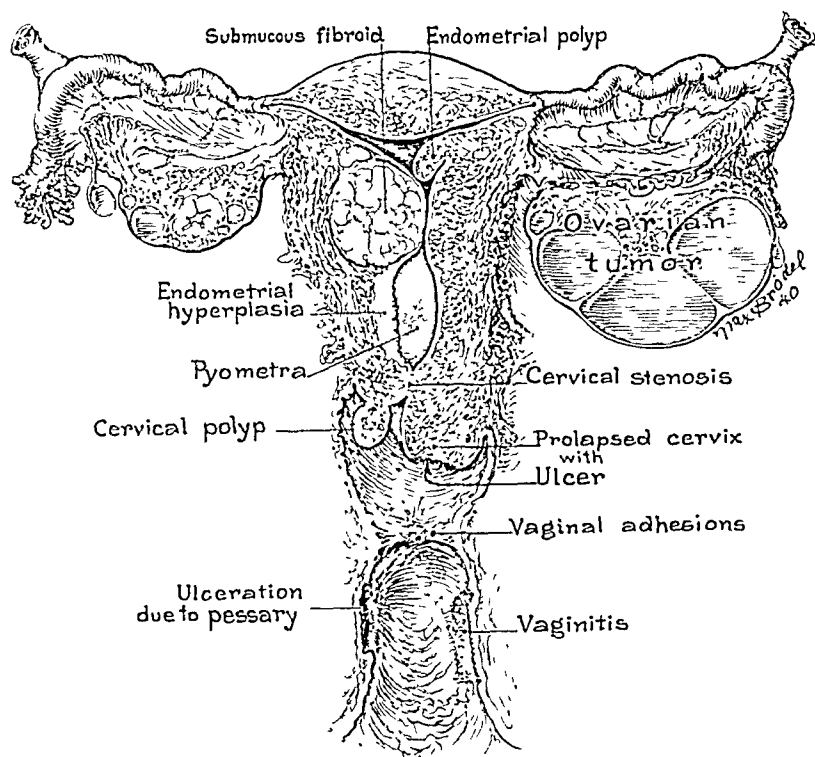


FIG. 2. Diagrammatic chart illustrating benign causes of postmenopausal bleeding.

of this lesion. After the menopause, when the estrogenic hormone is withdrawn the effect of this is usually readily noted on the vaginal mucosa. The rugae become smooth and the epithelial lining becomes much thinned. In the sexually mature woman prior to her menopause the stratified squamous epithelium is 25 to 50 cell layers deep. The mucosa is a dull pink in color due to the heavy epithelial layer covering the blood vessels. This epithelial layer protects the subadjacent tissues from infection. After the menopause the epithelial wall of the vagina is much reduced in thickness. Consequently the blood vessels lying beneath the epithelium give the vagina a redder color. This thin epithelium is easily subject to abrasion and the small abrasions serve as portals of entry for the ever-present vaginal flora. Vaginitis results and produces a discharge which, because of the abrasions, is often blood tinged. Not infrequently in elderly women, in whom

coitus or on exertion may on occasion cause bleeding which, at times, is quite profuse. This bleeding can be frequently demonstrated in the office by breaking the adhesions digitally.

Cervical polyps were responsible for postmenopausal bleeding in 6.6 per cent of the cases. Such polyps are no respecter of age. We have never seen one before the beginning of menstrual life, but they do occur at any time before the menopause and also after it. They invariably become infected and often ulcerated. The spotting which frequently appears after coitus or on straining is rather characteristic of an ulcerative lesion on the cervix and often is the first sign of cervical cancer. The finding of a polyp after obtaining such a history is indeed fortunate. All cervical polyps should be removed and biopsied, but the incidence of carcinoma in them is very rare. They are frequently the site of epithelial metaplasia producing cancer-like lesions. A follow-up



study of a group of these cases has proved to us that they are benign. Their greatest importance lies in the necessity of their recognition as benign lesions and in thus preventing unnecessary radical surgery. I am convinced that hundreds of pan-hysterectomies are done annually in the United States because of erroneous interpretation of these microscopic pictures.

Cancer-like epithelial changes are not limited to cervical polyps. With the profession becoming more "cervical inspection conscious" more biopsies are taken and hence more of these suspicious lesions are seen. Their proper interpretation becomes increasingly important with their increasing number. It is not within the scope of this paper to elucidate the finer histologic changes. Suffice it to say that every bit of tissue removed from the cervix for diagnosis should be examined by a competent gynecological pathologist, bearing in mind that many competent general pathologists are not expert in the gynecological field.

Endometrial polyps also occasionally occur after the menopause and cause bleeding. A curettage usually stops the bleeding, at the same time establishing a diagnosis. A polyp, however, is often brought away so minced up that it cannot be recognized as such in the curettings.

Endometritis occurring after the menopause may be responsible for bleeding from the atrophic uterine mucosa. The cause of the infection is not always apparent but in many cases a definite stenosis of the cervical canal can be demonstrated. Adhesions in and constrictions of the cervical canal may more or less completely occlude it after the termination of menstrual life. Apparently this condition often persists for years, causing no symptoms, but in some cases the lack of drainage from the uterine cavity results in pyometra formation due to infection of postmenopausal secretion of the endocervical or endometrial glands. When the intra-uterine pressure reaches a certain point the adhesions rupture and there is a vaginal discharge of blood tinged purulent material. The adhesions may form again and the discharge stop, only to

reappear when the pus in the uterus increases the pressure to a sufficient degree to rupture them.

In 4.4 per cent of our cases nothing was found to explain the bleeding other than fibroids. Since fibroids are present so commonly after the mid-thirties the question is naturally raised as to whether those found after the menopause are merely incidental findings or whether they are the cause of the bleeding. In our series fibroids were found in the uterus in many instances in which there was another obvious cause of bleeding. Those, we regarded as incidental findings and we will not consider them here. In about a third of the cases in which fibroids were the apparent cause of bleeding, sarcomatous change had taken place in them. The breaking down of tissue incident to this discharge obviously was responsible for the bleeding. In most of the other cases the myomata were of the submucous type projecting into the uterine cavity. The question arises whether these occupied the submucous position before the menopause or whether they progressed toward the cavity later. From examining the specimens it would seem that in many cases they scarcely could have been in their submucous position without having caused profuse bleeding before the menopause which would have necessitated their removal. In many of the cases several years had elapsed since the menopause without bleeding. It would seem reasonable, then, to assume that an intramural fibroid which is present before the menopause may work toward the uterine cavity after the menopause and bleed. From a clinical standpoint the important thing to bear in mind is that when a woman with postmenopausal bleeding presents herself and fibroids are found, one has no right to consider the fibroids the cause of the bleeding and defer a complete investigation. More often than not, the fibroids will be found to be incidental and the investigation will reveal some other lesion as the source of the blood.

The relation of ovarian tumors to postmenopausal bleeding is an important one. In about one-fourth of our ovarian tumors

which occurred after the menopause there was uterine bleeding. Often bleeding is the first symptom which calls the patient's attention to the fact that all is not well with her pelvic organs. Ovarian tumors of various types may be present. The appearance of blood from the uterus in the presence of an ovarian tumor is no indication of the histologic nature of the ovarian growth. About half of the ovarian tumors associated with uterine bleeding were benign and approximately half were malignant. The manner in which these ovarian growths cause bleeding is not always apparent. With malignant tumors extension of the growth to the uterine cavity, directly or via the tubes, frequently explains the bleeding. In benign growths, however, such as cystadenomas, no such explanation is possible and there is no evidence that these tumors have a hormonal effect. In the relatively rare granulosa cell tumors there is every reason to believe that the estrogenic hormone is produced in them. This belief is based upon several bits of evidence: the increase in size of the postmenopausal uterus to that of a woman in active menstrual life; the almost constant presence of endometrial hyperplasia in the endometrium; the occasional evidence of breast hypertrophy; and the production of estrus in spayed laboratory animals in which such tumor tissue has been implanted.

In a small group of women with bleeding after the menopause no pathologic lesion can be demonstrated in spite of careful and thorough investigation. It has been suggested by some that hypertension and arteriosclerosis may be responsible for the rupture of endometrial vessels with resultant bleeding. The term uterine apoplexy has been suggested as descriptive of these cases. The idea is attractive, but there are no convincing pathologic data to substantiate it. In our series, in the group with bleeding not explained on an obvious organic basis, the average blood pressure was not abnormally high and we are inclined to be skeptical concerning the hypertension-arteriosclerosis theory.

After considering the pathologic lesions which may cause postmenopausal bleeding it becomes apparent that a knowledge of pathology is the bedrock upon which good gynecology is practiced. The procedures required for a pathologic diagnosis are usually obviously indicated. Each case requires a careful bimanual examination and an equally careful inspection of the vaginal and cervical mucosa through a speculum with adequate illumination. If these procedures do not clearly demonstrate the source of the bleeding a diagnostic curettage and often a cervical biopsy must be done. When this is carried out very careful bimanual palpation of the ovaries should be done under anesthesia. If no lesion has been found adequately to explain the bleeding after these procedures, the patient should not be lost sight of but should return at frequent intervals for reexamination. If subsequent examination shows evidence of ovarian enlargement a laparotomy is indicated. If the bleeding persists after curettage and the cause has not been satisfactorily demonstrated a laparotomy is indicated, providing the physical condition of the patient is satisfactory. In some instances in which this has been done, ovarian neoplasms too small to be detected bimanually have been found to be the cause of the bleeding.

#### SUMMARY

A clinical and pathologic study of bleeding after the menopause shows that in more than half the patients the cause of the bleeding is malignancy of the generative tract. This being a proved fact, the logical deduction is that a complete investigation of each case is imperative. In many cases this includes an examination of biopsied tissue by a competent gynecologic pathologist. There are, it is true, many benign causes of postmenopausal bleeding, most of which are easily cured, but pathologic studies indicate that the only safe assumption is that malignancy is responsible for the bleeding until unequivocally proved otherwise.

# OFFICE TREATMENT OF THE PATHOLOGIC CERVIX\*

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NOT so long ago, effective treatment of the pathologic cervix usually meant hospitalization and surgery. Today we can effect cures in the majority of cases with greater efficiency by treatment in the office, without crippling the cervix, and with minimal discomfort and expense to the patient.

This paper will limit itself to the office treatment of nonspecific infections and benign lesions of the cervix. The lesions to be considered are: erosions; endocervicitis; lacerations with eversion and/or erosion; cysts; polyps; strictures; stenoses; leukoplakia; endometriosis; varicosities; "strawberry cervix." The anatomy, physiology, and pathology will be reviewed briefly in order to understand the treatment of these conditions more clearly.

The cervix is the lowermost portion of the uterus, extending from the external os to the internal os. It differs from the body of the uterus both in its anatomy and physiology, although it is developed from the same portion of the Müllerian duct.

The cervix may be divided into the infravaginal portion (*portio vaginalis*) which projects into the vagina, and the supravaginal portion (*portio supravaginalis*) which lies in the pelvic cavity, and is supported and encircled by that part of the connective tissue which forms the parametrium. Posteriorly this cellular tissue is part of the uterosacral ligaments, while anteriorly it extends along the less marked uterovesical ligaments. In the lateral parametric cellular tissue lie the uterine arteries and ureters within 2 cm. of the cervix. The parametrium also contains a rich network of lymphatic vessels which drain the cervix and furnish an easy road for the upward spread of infection.

The cervical canal is fusiform in shape, with an average length of 3 cm. (Fig. 1.) Along the midline of the anterior and posterior walls there is a longitudinal ridge from which a large number of oblique folds are given off (*plicae palmatae*) which by their inclination favor drainage downwards. The mucosa consists of a large number of compound racemose glands, more numerous towards the external os where they are branching and covered by high cylindrical goblet-cell type epithelium. Towards the internal os the glands are fewer, less branching, and the epithelium is low columnar, the nuclei are basal, the cytoplasm clear, and there is a basement membrane. These glands produce an abundant secretion of alkaline mucus, pH 7 to 7.5 which is clear, viscid, colorless, and empties through small ducts into the cervical canal. The epithelium lining the canal is continuous with the epithelium of all the glands which lie in the stroma. Due to this arrangement of rugae and numerous branching glands, the secretory area of the cervix is enormously increased, with a minimum of exposed surface, making the mucosa a forest of crypts, tunnels, and recesses. This epithelium partakes only to a slight degree in the cyclical changes so characteristic of the uterine epithelium, but it is not shed with the menses and therefore does not enjoy the advantage of being cast off and renewed.

At the proximal end of the cervical canal is the internal os where there is a sharp transition between the cervical and uterine epithelia. At the distal end is the external os, where normally the glandular epithelium ceases and stratified squamous epithelium begins, covering the *portio vaginalis*. The external os is encircled by

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the anterior and posterior lips, and is normally in close contact with the posterior vaginal wall.

**Erosion.** This is the most common lesion. It is seen as a bright red circular area of varying size, immediately surrounding the external os. It may be smooth or softly irregular to the touch, and may bleed easily on sponging. It is classified as simple, papillary or follicular depending upon the number and degree of the down-growth of the glandular element. This differentiation does not influence the treatment, and need not be discussed now. Although erosion is frequently referred to as "ulcer," it is actually covered by a single layer of columnar epithelium.

From the clinical standpoint, cervicitis may be divided into two groups: in one group, disturbance of physiology is the etiologic factor; in the other, which comprises most of the cases, the cause is infection.

In the first group, erosion is the only lesion, and the endocervical mucosa is normal in structure. The glands may function normally, or there may be excessive secretion. These erosions may be congenital or acquired. In a series of 500 cases of cervicitis in private practice Holden<sup>1</sup> found that one out of five occurred in unmarried women, eighty-five of these hundred patients having hymens so small and sharp edged as to be classed as verifiable virgins. (Fig. 2E.)

Wollner<sup>2</sup> has done some interesting experimental work showing that estrin has a stimulating effect on the growth of the columnar epithelium and progesterin stimulates the proliferation of the squamous epithelium, and the balance between these hormones has a direct bearing on the columnar-squamous cell proportions of the cervical epithelium.

In the group where infection is the cause, a small number are due to endocervicitis resulting from vulvovaginitis in childhood. In many of these, the cervix was infected by the hematogenous route as a complication of the exanthemata, particularly

scarlet fever.<sup>3</sup> Some of these childhood infections are gonorrheal in origin.

The greatest proportion of cases is found

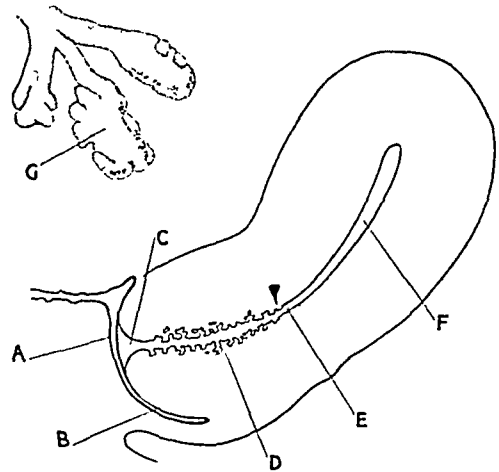


FIG. 1. Schematic drawing of the anatomy of the cervix. A, mucosa of vaginal vault in direct contact with B and C, external os surrounded by both lips. D, epithelium of cervical canal with its branching racemose glands. E, internal os. F, uterine cavity. G, single gland of cervical canal showing branching and crypts.

in parous women, in 50 to 80 per cent of whom erosions are found following delivery. In this group, the predominant organisms are staphylococcus, streptococcus, and *B. coli*. The gonococcus is responsible for another large percentage of cases, with the endocervical mucosa as the primary site for this type of infection. Secondary invaders often contribute considerably to the pathology, and may remain long after the gonococcus has disappeared. There may or may not be involvement of the portio as well. In private practice, the gonococcus is much less frequently seen as a cause of cervicitis than the nonspecific organisms.

Because of its anatomy, when the endocervical tissue becomes infected, the bacteria lodge in the crypts and lacunae of the racemose glands, causing a glandular proliferation, exudation, edema, vascular engorgement, polymorphonuclear, round and plasma cell infiltration. The hyperplasia and hypertrophy of the glands are accompanied by hyperfunction, resulting in an excessive amount of mucopurulent alkaline discharge.

The portio vaginalis with its stratified squamous epithelium accustomed to the acid medium of the vagina with its pH 4 or is normal in amount and character, the external os is again in an acid medium, giving the stratified squamous epithelium

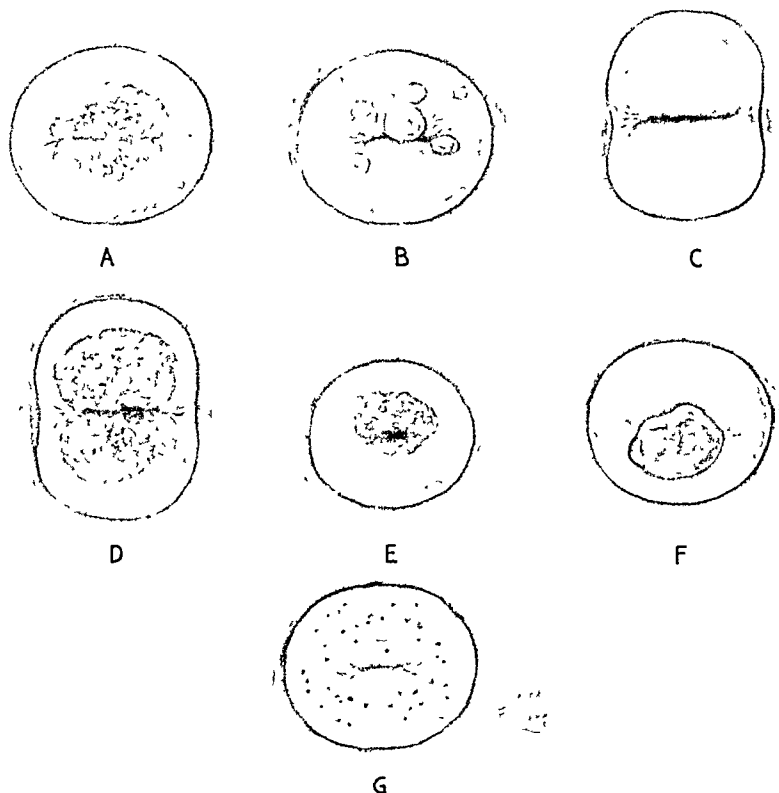


FIG. 2. Lesions of the cervix. A, erosion. B, Nabothian cysts. C, bilateral laceration healed. D, bilateral laceration with eversion and erosion. E, erosion in a virginal cervix. F, polyp. G, strawberry cervix.

4.5 thus lies in a pool of mucopus with an alkaline reaction of pH 6 to 7.5. In addition, the subepithelial area becomes heavily invaded by bacteria and cellular infiltration, often with small subepithelial hemorrhages. The squamous epithelium becomes raised, macerated, and in a short time the area surrounding the external os becomes denuded, forming a true erosion.<sup>4</sup> This lasts only a short time, for nature will make every effort to re-epithelialize. The columnar epithelium of the endocervix which can live in this alkaline medium, grows downward and over the denuded part of the portio, forming a bright red area covered by a single layer of columnar epithelium, which is the erosion as we see it clinically. (Fig. 2A.) When the infection is improved or cured so that the endocervical secretion

of the portio the upper hand. In the reparative process, the squamous epithelium displaces the glandular epithelium until the eroded area is entirely epithelialized with squamous epithelium and the erosion is healed.

Roblee<sup>5</sup> thinks that the vaginal pH is the primary factor in inducing erosions. In his series, cervixes subjected to a pH of 6.5 to 7.5 showed some columnar proliferation and an acute cervicitis. When the medium was then changed and maintained at pH 4 to 4.5, these same cervixes showed some squamous cell epithelialization with a retreat of the columnar epithelium.

*Nabothian Cyst.* In this process of destruction and repair, the duct of many a cervical gland becomes occluded so that its secretion has no exit. The accumulation of

this secretion forms a cyst which on the vaginal surface looks like a translucent pearly area. Rarely this will contain pus instead of clear mucus, forming a Nabothian abscess. Often these cysts are not visible, as they may occur deep in the portio or high in the canal.<sup>6</sup> When many of these cysts are found, the cervix is described as cystic. (Fig. 2B.)

*Lacerations* of the cervix are due to trauma, usually during labor, occasionally if too forceful a dilatation is done preceding curettage. The laceration may be unilateral, bilateral, or stellate. It may be small or large enough to extend outward into the parametrium. Lacerations usually heal spontaneously. A healed laceration is of no danger and needs no treatment. (Fig. 2C.) It requires attention only when complicated by chronic infection, erosion, or ectropion. Eversion or ectropion occurs in conjunction with a bilateral cervical laceration which allows the endocervical tissue to pout out into the vagina. (Fig. 2D.)

*Polyps* are caused by a hyperplasia of the endocervical mucosa. They are usually single, but may be multiple, and are pedunculated. They are usually accompanied by a low grade endocervicitis, and are easily seen and felt as soon as they extend to or beyond the external os. (Fig. 2F.)

*Strictures and Stenoses.* These lesions are frequently overlooked, and are usually a result of endocervicitis or of the treatment for this condition. Occasionally, they follow a poorly executed surgical repair or a very traumatic obstetrical delivery. Intrauterine radium therapy may lead to subsequent stenosis. Senile atrophy occasionally may cause stricture, and rarely complete occlusion. When these lesions follow cauterization, conization, or coagulation of the cervical canal, it is often due to the fact that the operator was not sufficiently familiar with the technique.

*Leucoplakia* is rare. It is a circumscribed irregularly shaped patch of white thickened mucosa, and is of importance because some believe it has malignant potentialities.<sup>7</sup>

*Endometriosis* is very rare and is seen as small endometrial transplants on the portio vaginalis and in the vaginal mucosa

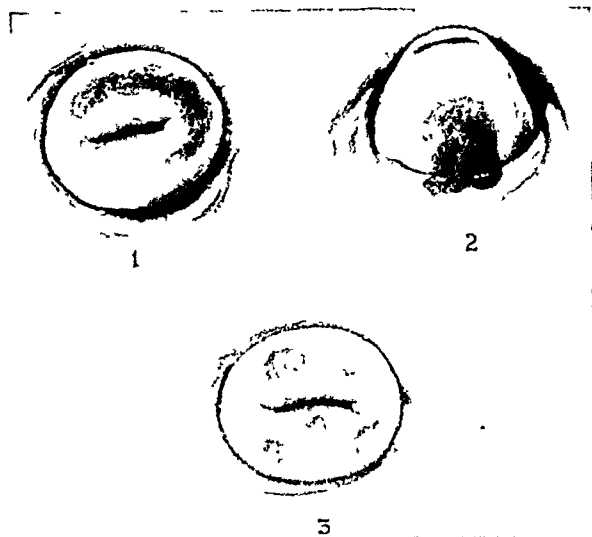


FIG. 3. Various types of superficial ulcerations seen in some cases of trichomonas vaginalis vaginitis. (From Kleegman, in *Surg., Gynec. & Obst.*, 51:552, 1930.)

of the vault. These transplants are  $\frac{1}{4}$  to 1 cm. in diameter, and look like dark blue Nabothian cysts.

*"Strawberry Cervix."* This term is applied when the epithelium of the portio is reddened and has numerous spots of a deeper red, so that the cervix looks like a strawberry. (Fig. 2G.) It is part of any acute vaginitis. In addition, superficial ulcers of the portio occasionally occur in acute trichomonas vaginitis. (Fig. 3.) It is not necessary to treat the cervix apart from the vaginitis, and the condition is mentioned here only to complete the picture.

*Incidence.* A pathologic cervix is the most prevalent of all gynecologic disorders and the anatomy of the canal almost precludes any spontaneous cure. Polak<sup>8</sup> stated that 85 per cent of all women had cervicitis. Fulkerson<sup>9</sup> in a review of 6,483 gynecologic records found a diagnosis of cervicitis made in 33.16 per cent; 80 per cent of these had been pregnant and 20 per cent had never been pregnant. We have found an incidence of cervicitis in 50 per cent of our private patients, 80 per cent of whom had been pregnant.

*Symptoms.* Leucorrhea is the most common and frequently the only symptom, occurring in 80 per cent of all cases. Usually it does not cause itching or irritation. There are no symptoms in 20 per cent of cases. Additional symptoms commonly present are backache, sense of weight in the pelvis, menorrhagia and metrorrhagia, dysmenorrhea and occasionally dysuria. Sterility<sup>10</sup> will follow when the purulent cervical secretion forms a mechanical barrier which the sperm cannot penetrate. This latter assumption should always be checked by means of the Hühner test.<sup>11</sup> When the infection extends in the cellular tissue along the uterosacral ligaments, making them thickened and tender, then backache and dyspareunia are the two common symptoms. Cervicitis is a potential focus of infection. In a small series Moench<sup>12</sup> produced acute arthritis in animals with streptococci which she isolated from cases of cervicitis. An occasional case of arthritis will be cured only after the cervical infection has been cured or removed.

Polyps and endometriosis of the portio will often cause pre- and postmenstrual and postcoital spotting. Varicosities, if marked, cause a sense of weight in the pelvis. A ruptured varix will cause bleeding. Leucoplakia causes no symptoms.

Stenosis will give a history of dull premenstrual pain, severe comenstrual pain at the height of the flow, with a prolongation of the period. If the stenosis has resulted from cervical treatment, the patient will date her symptoms since the procedure. Amenorrhea accompanied by considerable abdominal pain means complete obstruction. The sudden appearance of a profuse purulent discharge after the menopause is often due to a pyometra caused by cervical stricture.<sup>13</sup>

*Differential Diagnosis.* Erosions must be differentiated from carcinoma. In early cases this is very difficult, if not impossible. Schiller's<sup>14</sup> test consists of painting the eroded cervix with fresh Gram's iodine solution. This test is based upon the fact

that the vaginal cells are rich in glycogen, whereas carcinoma cells contain little or no glycogen. Benign lesions take a mahogany brown stain, whereas malignant tissue does not take the stain. This test is useful only as an aid, and cannot be leaned upon too heavily. Examination with the colposcope<sup>15</sup> is also only an aid. Nothing can take the place of expertly trained senses, aided by adequate exposure, good light and careful inspection in order not to overlook possible suspicious lesions. Biopsies must be taken of all suspicious areas. These should include some of the surrounding normal tissue and can be taken either with a biopsy punch or by the use of a thin wire loop electrode attached to a fast cutting current. After using the biopsy punch, it is well to sear the raw surface with the cautery. When a cervical erosion does not respond to the treatment to be described, always be suspicious of carcinoma and take a biopsy. It requires an expert pathologist to make a diagnosis of a biopsy specimen, especially in these early cases, otherwise a malignant lesion will be overlooked, or a benign lesion will be erroneously diagnosed as malignant.

Painless, bright red bleeding late in pregnancy may be due to a ruptured varix, an extensive erosion, or to a polyp. Therefore, with scant or moderate amount of bleeding, a diagnosis of placenta previa should not be made without adequate inspection of the cervix.

Syphilis of the cervix is difficult to diagnose. A chancre in its early stage may be easily mistaken for an erosion, since it is usually centrally located involving the external os.<sup>16</sup> When eccentric, the posterior lip is involved more often than the anterior lip. A little later, the chancre looks like a funnel shaped ulcer with a grayish membrane at its base, which when removed, bleeds very little and has little discharge. It is usually an accidental finding because it is symptomless and fleeting. Secondary lesions of the cervix have the same characteristics as secondaries anywhere else. Accompanying these lesions, there is an

enlargement of the sacral, lumbar, and hypogastric glands, and in some cases these can be palpated as discrete tender nodules posteriorly and laterally behind the broad ligaments. The diagnosis can be substantiated only by the positive dark field examination. Local treatment is useless, and valuable time may be lost if this condition is not borne in mind.

Gumma and tuberculosis of the cervix are very rare. They are usually mistaken for carcinoma, and the diagnosis is made only on examination of a biopsy specimen.

*Prophylactic Treatment.* Artificial dilatation of the cervix, or forcing a fetus through a rigid undilated cervix either by traction or injudicious use of pituitrin may cause extensive lacerations. When the surroundings are aseptic and the patient is in good condition De Lee<sup>17</sup> advocates inspection of the cervix under good light and adequate exposure immediately after delivery, and repair of all cervical lacerations. Hasty and traumatic cervical dilatation preceding a curettage may also cause laceration.

Reduction of gonorrhea by education and prophylaxis would reduce cervical infection tremendously.

Discovering the cervicitis is an important step in the prophylaxis. With increasing education in preventive medicine, more and more women are coming to the physician for yearly physical examination. The pelvic organs are usually excluded from this check-up by a large percentage of physicians. No woman has had an adequate survey without a gynecologic examination, including careful inspection of the cervix. With the proper mental attitude of doctor and patient, and with suitable instruments and the necessary experience this could readily be done even through the undilated hymen in almost all cases. I do not advise routine vaginal examinations of the young girl, but when dealing with the mature woman who comes to see "if she's all right," there is no excuse for ignoring such an important part of her body as her generative organs. In women who have had

a supracervical hysterectomy, it is equally important to examine and carefully inspect the cervical stump at regular intervals.

Adequate postpartum care is another important measure. Even in this group the cervix is often overlooked. Despite good obstetric care, labor is still one of the important etiologic factors in initiating cervical pathology. Of all women examined in the postnatal period, 50 to 80 per cent require some cervical treatment.<sup>18</sup> The present custom of discharging the woman after one examination six weeks postpartum is inadequate care. In many instances a cervix may look fairly healthy at this time and the uterus may be in good anteversion, yet when the same patient is seen three to four months postpartum the cervix may present an erosion and the uterus may be found in retroversion. Patients should be seen six weeks, two, four, and six months postpartum in order to make sure the cervix and uterus are in good condition and position.

All authorities agree that carcinoma does not occur in a healthy cervix, and although the word "precancerous" is looked upon with disfavor, pathologists nevertheless consider cervicitis a precancerous lesion. All large studies confirm the view that the most important and effective means of treating cancer of the cervix is to prevent its occurrence by curing the lesions of the cervix while they are benign. Dickinson, Holden<sup>19</sup> and others have not seen carcinoma arise in any case of cervicitis that they have treated. In this country, 16,280 women died of carcinoma of the uterus in 1936, 80 per cent being of cervical origin. These deaths could be reduced greatly by proper care of the cervix. In order to give appropriate treatment, a complete physical examination must include careful inspection of the cervix.

#### TREATMENT

*Chemical Treatment.* Topical application of large numbers of various chemicals has been and still is for the majority of practitioners the method of choice in



treating cervical pathology. This should not be so, for in most instances, the chemical treatment is inefficient and unduly

suppository.\* In a preliminary report of a series of ninety-seven cases of cervical erosions treated with topical applications

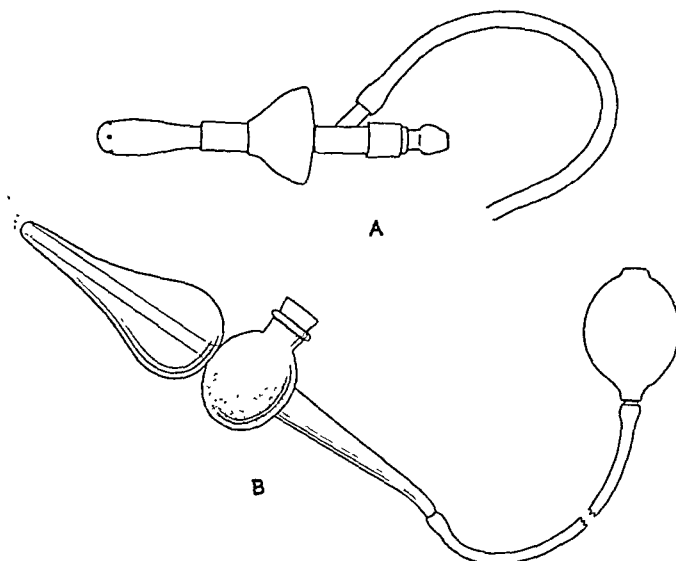


FIG. 4. A, douche point. Conical collar is movable, and with inflow and outflow circuit vagina can be distended, making douche more effective. B, powder blower. Vaginal outlet can be closed so that with pressure the vagina is distended, allowing the mucosa and especially the vault to become thoroughly powdered.

prolonged. Referring back to the anatomy of the endocervical mucosa, one can realize how futile it is to try to cure a chronic infection of these glands with topical applications or douches. There are two classes of exceptions to this statement. In cases of acute erosions, where thermal or electrical measures are contraindicated, painting the erosion with a chemical has its place. In other cases where the infection is only superficial and can be quickly cured by a surface attack, topical application of a chemical may be indicated. The favorite drugs in use are various silver preparations, mercurochrome, aniline dyes and tincture of iodine.

For the past two years in the Bellevue Hospital clinic and in private practice we have treated cervicitis with a product called negatol. In our experience, we have found this superior to the foregoing chemicals mentioned. Negatol is an aqueous solution of the colloidal products formed by reacting cresol sulfonic acid with formaldehyde. It comes as a liquid, powder, or

of 100 per cent negatol solution twice weekly, 69 per cent were cured, 24 per cent improved and 7 per cent unimproved. The average number of treatments was seven, over an average period of time of fifty days. In 20 per cent of the cured cases the erosions were graded as of severe degree.<sup>20</sup>

However, negatol is not so effective as the electrical methods to be discussed, and has a place only when these more efficient measures are contraindicated.

**Caustics.** Local applications of caustics, such as chromic acid crystals<sup>21</sup> and caustic potash crayon<sup>22</sup> likewise are not so effective. They result in a higher percentage of cervical stenoses, and have been discarded by us.

**Powders.** Based on his work with vaginal acid-alkali relationship to cervical erosions, Roblee<sup>5</sup> has cured superficial erosions by maintaining the vaginal acidity continuously between pH 4 and 4.5. This he does by having the patient insert

\* Supplied to us for experimental purposes through the courtesy of Eli Lilly Co.

nightly a gelatine capsule containing 12 c.c. of a powder mixture of B lactose 80 per cent and boric acid 20 per cent. The pH of the vaginal secretion can be tested with sufficient accuracy by using fresh nitrazine paper as an indicator.<sup>23</sup> Vinegar douches (2 ounces to 2 quarts) are taken only after coitus and during the menstrual period, the instillations of the powder being continued after such douching. A more efficient means of powdering the entire vaginal mucosa, especially the region of the vault, is to insufflate the powder by means of a vaginal powder blower. (Fig. 4.) Here again, this treatment is more tedious, and often less effective than the electrical methods. Roblee states that simple erosions will respond to this treatment, but that it is insufficient to cure papillary or follicular erosion. The value of the method lies chiefly in that the patient can carry on the treatment herself; it is also helpful where electrical methods of treatment are contraindicated.

Injection of various chemicals into the cervix,<sup>24,25,26</sup> medicinal pastes<sup>27</sup> and ionization treatment<sup>28</sup> whereby metal ions are forced into the cervical tissues have been recommended by various isolated workers. We have no personal experience with them.

*Electrosurgical Methods. Thermal Treatment.* From the earliest antiquity, heat in one form or another has been held in high esteem as a therapeutic agent. Nearly every type of lesion or wound has been treated with the hot iron. Hippocrates used fire for healing. In 1811 Percy recommended treating the ulcerated cervix with a glowing iron, and this was carried out in 1843 by De Lambelle. In 1906, Hunner<sup>29</sup> used the Paquelin cautery in the treatment of endocervicitis. In 1911, Dickinson<sup>30</sup> began the treatment of cervicitis with the fine wire nasal tip cautery, and this method has proved to be the safest and most effective for the largest percentage of cervical lesions.

We have discarded the use of the heavy duty electrical cautery, the Paquelin

cautery, and the Post cautery, as the heat is not sufficiently restricted, and too often extensive scar tissue with subsequent stenosis is the result.

*Cauterization of Cervical Erosions, Nabothian Cysts, Endocervicitis, Polyps, Endometrial Transplants, Cervical Varicosities by the Nasal Tip Cautery Points.* This form of therapy has been the greatest advance in the treatment of cervical pathology, since the method is technically the simplest and most foolproof. The apparatus required is the least expensive of any of the electrical methods, few treatments are necessary, and the results are excellent. The necessary experience can be easily acquired by any physician, and the possibility of complications is by far the least of any method of treatment.

However, damage can be done unless the proper technique is employed. There are likewise contraindications which pertain to all the electrical methods to be described.

*Contraindications.* Cauterization should not be done on an acutely infected cervix, nor in the presence of acute or subacute pelvic pathology. If these contraindications are not heeded, serious and extensive pelvic infection may flare up as a result, occasionally resulting in death. This is especially true in the presence of an acute streptococcus infection. We do not cauterize when spreads are positive for gonococci. However, Goldblatt<sup>31</sup> treated 2,627 cases of gonorrheal endocervicitis by means of electrocoagulation and/or conization, twenty of whom were from one to nine months pregnant. He claims that the acuteness of the infection was no contraindication and did not affect the healing. The twenty pregnant patients all went to full term and had uneventful deliveries.

*Technique.* The apparatus needed consists of rheostat, a handle, and an electrode. The electrode should have shanks 6 to 8 inches long with tips of various shapes made of platinum fine wire. (Fig. 5.)

Good exposure of the cervix and good light are essential. It is not necessary to use a tenaculum.

To cauterize an erosion, no anesthesia is required, even on the nervous patient, as the portio is insensitive. Cleanse the cervix

thoroughly dry before the speculum is withdrawn. To stop oozing, the heat is reduced to so low a point that the tip barely glows,

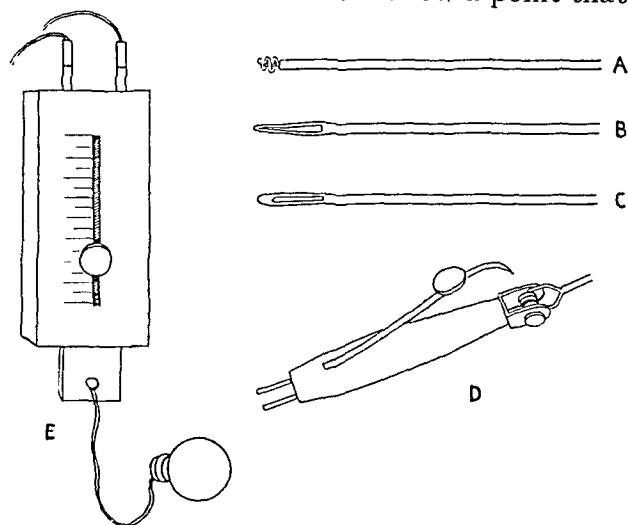


FIG. 5. Armamentarium for nasal tip cauterization. A, B, C, different types of cauterization tips. Only the terminal tip heats up, the handle remaining cold, so that the heat is restricted to the point of application. A, corkscrew for endocervical cauterization. B, pointed tip for Nabothian cysts, varicosities, and endometrial transplants. This may also be used for erosions. C, blade tip for erosions and removal of polyps. D, handle. E, rheostat.

with peroxide or tincture of green soap. Dry. With the blade tip heated to a bright red, cauterize the posterior lip first, starting from the external os to the outer margin of erosion. The strokes should be slow, even, about 2 to 4 mm. deep and 0.5 to 1 cm. apart. The same procedure is carried out on the anterior lip, starting from the outer margin of the erosion and extending down to the external os, but stopping short of it so that no two cauterized stripes on apposed lips are left in direct contiguity with each other. This will avoid possibility of stricture. (Fig. 6.)

**Bleeding.** In gauging the heat of the tip by its color, the light of the surroundings must be taken into account. In a brightly lighted room a bright red tip may look dull red. Therefore the heat of the tip should be estimated in dim light (under the table is usually an accessible place). The patient should not see the cauterization point. Too much heat will burn out the tip, or may cause bleeding. The cervix should be left thor-

oughly dry before the speculum is withdrawn. To stop oozing, the heat is reduced to so low a point that the tip barely glows,

then the tip is held directly against the oozing point until the latter is seared and thoroughly dry. If any point is allowed to continue to ooze, it may give rise to troublesome bleeding subsequently.

Very rarely, oozing may begin about seven or ten days after cauterization when the slough separates. All oozing points can be stopped promptly with the above procedure. We have never found bleeding a problem with this type of cauterization.

If the canal needs to be cauterized, it should be well cleansed and dried first. The most effective means of getting rid of the thick cervical secretion is by the use of caroid powder. A cotton applicator dipped in this powder is rotated in the canal, the mucus is digested by the powder, and the canal is cleansed of all secretion. The canal is sensitive, and good anesthesia is obtained by inserting one or more cotton applicators saturated with 10 per cent novocaine solution, to remain for ten minutes. This at the same time will stop all oozing which the caroid powder may have started.

For this work either a straight or corkscrew electrode is chosen. Experience will guide the choice. With a widely open

surfaces are left in direct apposition. This means that only one-half of the canal surface is cauterized at the same sitting,

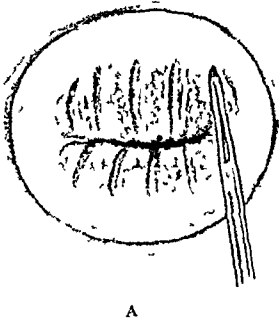


FIG. 6.

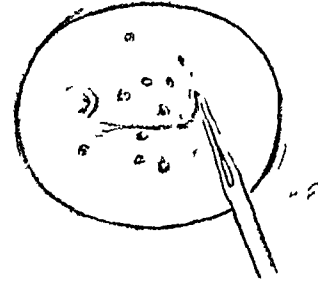
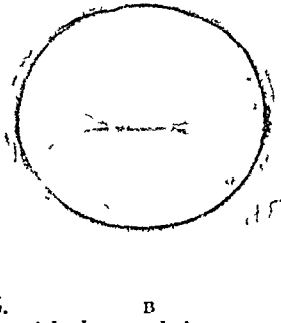
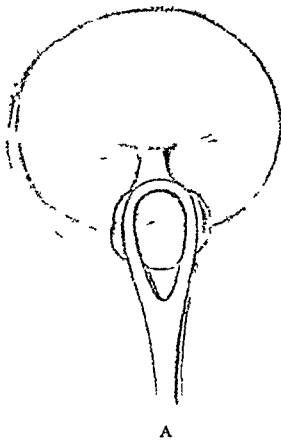


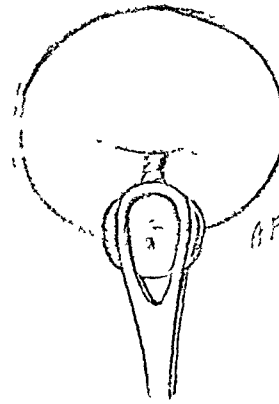
FIG. 7.

FIG. 6. A, cauterization of an erosion with the nasal tip cautery. The posterior lip has been cauterized and the last stroke is being made on the anterior lip. Stripes on both lips are made from above downward. Note that the stripes on the anterior lip do not extend as far into the external os as those of the posterior lip, so that raw areas of the lips will not come in apposition. B, end result after a total of four visits. Cauterization was done twice.

FIG. 7. Cauterization of Nabothian cysts with straight tip. The cyst wall must be destroyed.



A



B

FIG. 8. A, polyp grasped and traction applied. In actual practice, the pedicle is grasped much higher, as close to the base as possible. B, combined traction and rotation until polyp is twisted off, after which the base is cauterized.

external os, the straight tip may be better, while with a small external os, the spiral tip is usually preferable. With a small external or tight internal os, the canal should be gently and gradually dilated up to the size No. 10 to 12 with the Hegar's dilators. The degree of heat is chosen, the tip put in cold and then the heat turned on. The heat is again turned off before the tip is withdrawn. This will prevent undue cauterization of the external os. The cauterization is done with linear strokes from above downward, with care, especially in the region of the internal os, that no raw

the other half being done when the first has healed. If these simple precautions are taken, there will be no resultant stricture or stenosis as a result of this type of cauterization. (Fig. 9c.) Cauterization is best done four to six days after menstruation.

*Undercauterize rather than overcauterize.* All contraindications to cauterization should be heeded.

*Nabothian Cysts, Endometrial Transplants, Cervical Varicosities.* For the cysts, a sharp pointed electrode is used, the current turned on, and the tip plunged into the cyst. This may have to be done several

times in order to get rid of the collected mucus, after which the cyst wall is cauterized until completely destroyed. (Fig. 7.)

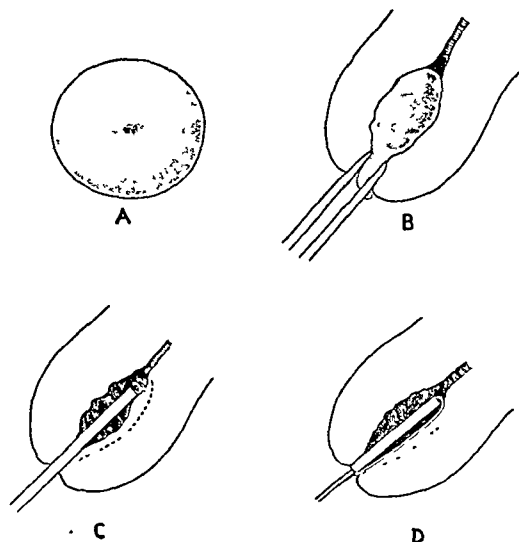


FIG. 9. Endocervicitis. A, there is no erosion and the cervix looks apparently normal. B, on introducing a uterine dressing forceps through the external os, and separating the blades, it is seen that there is a thick mucopurulent discharge filling the canal. This is the type of cervicitis that causes sterility. C, the canal has been cleansed, dried, and anesthetized. The corkscrew tip is inserted to the internal os, the current turned on, and the tip slowly drawn downwards as outlined, cauterizing the indicated strip of mucosa. The current is turned off before the tip is removed so as not to burn the external os. Three such stripes are burned parallel to each other over one-half the circumference of the canal. The other half is similarly cauterized six weeks later. D, Hyam's conization. The canal is similarly prepared, but the degree of anesthesia is greater. The current is turned on, the electrode introduced up to the internal os, then a complete circle made as the wire cuts through the mucosa of the canal, coring out the endocervical mucosa.

Many of these cysts are invisible, occurring higher up in the cervical canal, and are found accidentally while cauterizing the canal.<sup>6</sup>

Endometrial transplants and varicosities in the cervix are cauterized until completely destroyed, in a manner similar to that described for the Nabothian cysts. For varicosities, a dull red heat should be used.

**Polyps.** If the pedicle is thin, as it usually is, grasp the pedicle close to its source with a sponge stick or curved clamp, and with traction, rotate the polyp on its

pedicle, twisting it off. This is a simple procedure, and usually there is no bleeding. (Fig. 8.) The site of origin is then cauterized

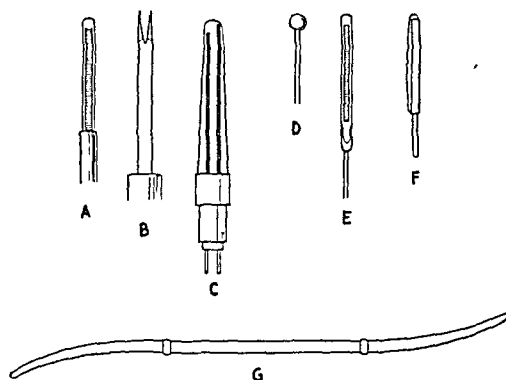


FIG. 10. Armamentarium for electrocoagulation and conization. A, Cherry electrode. There is a similar strip on the other side of the electrode so that opposite sides of the canal become coagulated at the same time. B, bipolar tip for cysts and erosions. C, Ende electrode. Here only the tissue between the two strips is coagulated, making it possible to control the area done at one sitting. D, ball tip electrode used by Barrett for electrocoagulation of erosions. E, tip used for coagulation of canal. Here there is only one strip as shown, so that the area treated can be controlled. F, Hyam's tip for conization of canal. These come in several lengths and shapes to fit various types of canals. G, Hegar's dilator for dilatation of the cervical canal.

with the straight or corkscrew nasal tip cautery. If the pedicle is thick, it is grasped, pulled downward, and severed at its base by slowly cauterizing with a dull heat, using the straight electrode. Care is taken to preserve the polyp during removal, as all polyps are routinely subjected to microscopic examination to avoid overlooking an occasional case of malignancy.

Erosions may be cauterized and polyps removed during pregnancy. Cervicitis increases puerperal morbidity,<sup>32</sup> and may safely be cleared up in the antepartum period. Since the majority of spontaneous abortions occur in the first trimester of pregnancy, it is wise to postpone this therapy until after the third month and thereby avoid the undeserved blame of a possible coincidental spontaneous abortion. Because of the greatly increased vascularity of the tissues, a low degree of heat

(cherry red) is used, and we have had no untoward results in any of our pregnant cases.

first two weeks. After the first week, the patient may douche if she wishes to, with some cleansing solution such as 1 ounce of

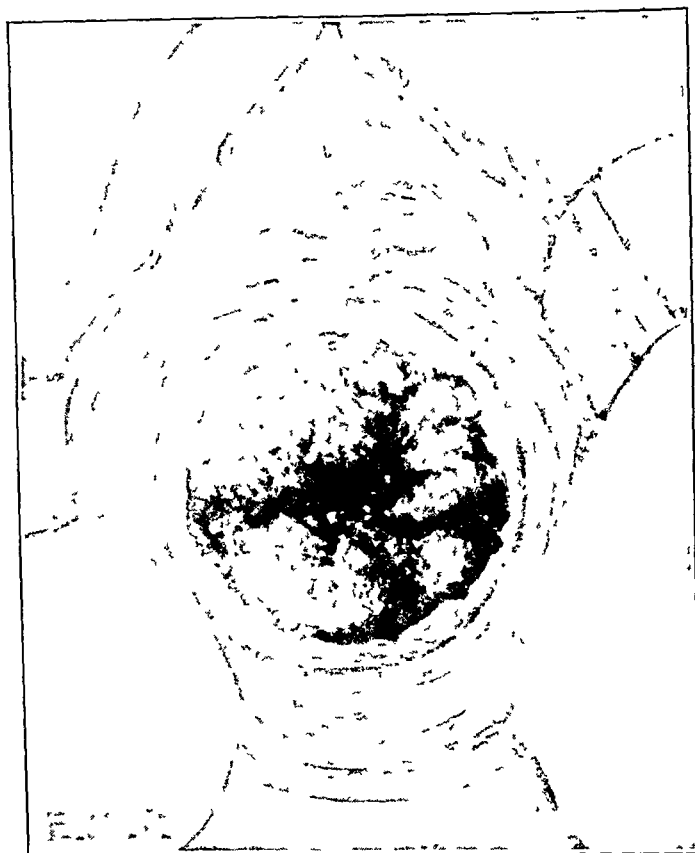


FIG. 11. Primipara eight weeks postpartum; before treatment. Note lacerations and extensive erosion. (From life drawing.) (From Barrett, in J. A. M. A., 103:1516, 1934.)

*After-Treatment.* The patient is seen two weeks, four weeks, and six or eight weeks after cauterization. Two weeks after cauterization the slough will be cast off, or is ready to be removed, leaving a raw area. This area is cleaned with peroxide or tincture of green soap, dried and a topical application made with 100 per cent negatol solution. This treatment is repeated two weeks later. Six to eight weeks after cauterization healing has taken place. If there are any unhealed areas of the portio or canal, these can now be recauterized.

The patient is warned that following cauterization she will have a profuse discharge, frequently blood tinged, for a period of two weeks, after which it will rapidly subside. Coitus is interdicted for the

tincture of green soap or 2 ounces of vinegar to 2 quarts of warm water. Many cases are cured with one cauterization, some require two, and only the occasional case will need more. We do not recauterize until at least six weeks and preferably eight weeks after the previous cauterization.

This is the method in use in the Gynecological Clinic at Bellevue Hospital, and is most commonly used in our private practice as well. We have found no method superior to the nasal tip cautery for the cure of erosions. Healing takes place without formation of scar tissue and the area is covered with normal squamous epithelium. In my personal series covering thousands of cases, there have been no complications nor untoward results.

For endocervicitis, there are a small group of cases where electrocoagulation and conization give results superior to the

left in the canal for forty-eight hours after this procedure. The other half of the canal is treated eight weeks later. When neces-

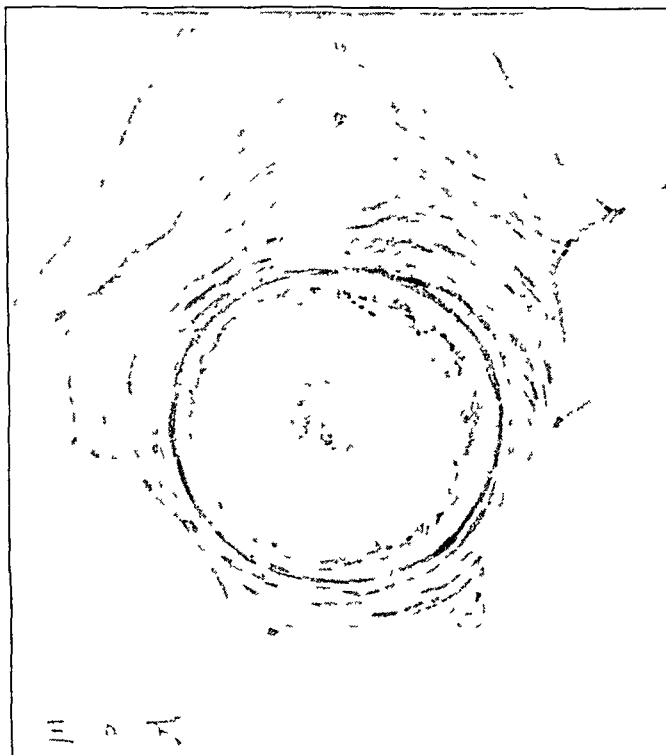


FIG. 12. Immediately after electrocoagulation. Note white coagulum. (From life drawing.) (From Barrett, in *J. A. M. A.*, 103: 1516, 1934.)

nasal tip cautery, particularly where there is a small external os, with a ballooned out chronically infected endocervical mucosa beyond it. (Fig. 9 A and B.)

**Electrocoagulation.** For this it is necessary to have a diathermy or radio tube machine and electrodes. Ende<sup>33</sup> devised a good one, and Cherry<sup>34</sup> has a modification of the Ende electrode. One disadvantage of the Cherry electrode is that, because of the placement of the metal strips, raw surfaces are left in apposition and the possibility of subsequent stenosis is increased. After the canal is cleansed, dried and anesthetized as previously described, the electrode is inserted into the canal, pressed against the wall and the current turned on for the required dosage. The handle is gradually rotated until a coagulation of half the canal is obtained, 2 mm. in depth. Ende recommends that a gauze soaked in enzymol be

sary, treatment may be repeated at eight week intervals. For erosions and cysts, the bipolar electrode is used, and the superficial tissue between the tips coagulated. (Fig. 10.)

For electrocoagulation of cervical erosions and endocervicitis in the late puerperium, Barrett<sup>35</sup> prefers the radio tube machine with ball tip electrode causing electrocoagulation of the eroded area. (Figs. 11, 12 and 13.) Workers using this method have corroborated his excellent results. In a small series of extensive erosions of both lips, I have treated one lip with the nasal tip cautery and the other lip with Barrett's method and have found healing the same in both lips as to time and degree.

**Conization.** Hyams<sup>36</sup> devised a technique whereby the infected glandular tissue in endocervicitis can be quickly

excised, analogous to the Sturmdorf<sup>37</sup> operation both as to tissue removed and degree of healing obtained. By means of his

excellent anesthesia, even for the nervous patient. In applying cocaine hydrochloride solution to the cervical canal, there have

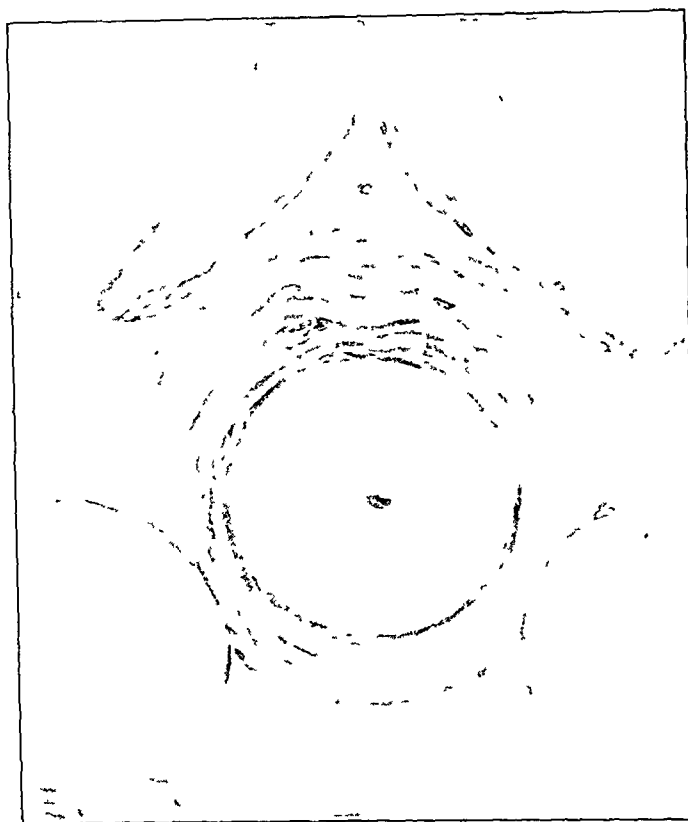


FIG. 13. Six weeks after electrocoagulation. Note normal appearance of cervix. (From life drawing.) (From Barrett, in *J. A. M. A.*, 103: 1516, 1934.)

electrode with a fast cutting current, Hyams cones out the mucous lining of the cervical canal and its glands without injury to the underlying musculature. It is an office procedure and when properly done, as simple for the patient as any of the others.

**Armamentarium.** The apparatus needed includes a diathermy or radio tube machine which can generate a fast cutting current, an inactive electrode 6 by 6 inches with a sandbag to hold it in place, and special electrodes of varying size and shape with silicon tip and a tungsten wire for cutting. (Fig. 10F.)

**Technique.** The canal is cleansed and dried. One or more cotton applicators saturated with 35 per cent cocaine solution are placed in the canal for ten minutes, as this method requires a greater degree of anesthesia than the others. This gives

been no reactions even though 35 per cent or 50 per cent solutions are used routinely. The cervical canal is the only orifice where such concentrated solutions of cocaine may be used with impunity. The tip selected depends upon the length and shape of the canal. The inactive electrode is moistened, placed upon the lower abdomen, held there by a sandbag and the patient is directed to make firm pressure on the sandbag, merely to divert her attention. The current is turned on to the proper degree, having just previously been tested on raw meat. With the current on, the silicon's end is passed into the canal to the internal os (Fig. 9D), the spark cutting through the tissue, and the tip is rotated through 360 degrees, coning out the entire epithelium lining the canal. It is helpful to use a bakelite speculum, but if a metal speculum is used,



do not let the tip come in contact with the speculum, as the tip will be destroyed. Hyams packs the canal and vagina lightly

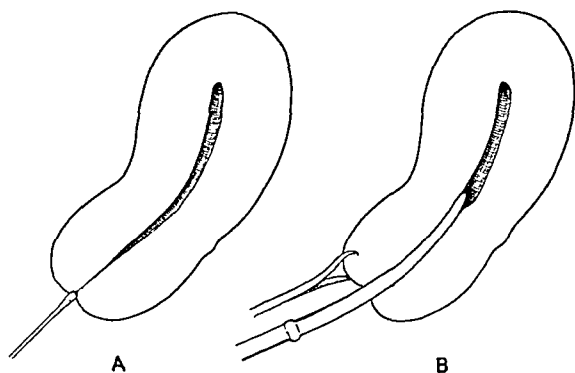


FIG. 14. This patient complained of severe dysmenorrhea and prolonged periods since conization of cervix two years ago. When first seen (A) a probe could barely be forced through the external os and canal. B, anterior lip grasped with tenaculum, external os gradually dilated to admit applicator soaked in 35 per cent cocaine solution. Graduated Hegar's dilators introduced up to No. 8 on first treatment, and to No. 12 on second treatment a month later. Periods painless and of her normal three days' duration since the first dilatation.

with gauze soaked in 1 or 2 per cent mercurochrome solution, which is left in overnight.

The after-treatment is the same as for the other methods, except that it is necessary to dilate the canal regularly during and after healing to prevent stenosis. This method is superior for the deep-seated endocervical infection of long standing.

Although the technique is easily learned, it should not be tried even by the expert gynecologist until he acquires experience with this particular method. I have seen instances of severe stenosis and know of other cases of severe hemorrhage necessitating hospitalization and transfusion. The fault is due not to the method but to its application, for in a large series of his own cases, Hyams reports no hemorrhage, no stenoses, no strictures. Knowledge of the appropriate voltage and amperage to be used is essential. Too great a heat will cause excessive carbonization and subsequent stenosis. Too fast a cutting current will cause hemorrhage. The current to be used should be checked on raw steak before each operation.

In my series of less than one hundred cases, there were four complications. One patient developed an acute pelvic infection principally of the left tube and ovary, mild in degree, which cleared up in two weeks with palliative measures. She had a long standing chronic endocervicitis with no history or evidence of gonorrheal infection nor adnexal disease prior to the conization. Three patients had profuse oozing. These were controlled by tight cervical and vaginal packing which was left in place for forty-eight hours. There were no subsequent stenoses nor strictures.

Jacoby<sup>38</sup> followed up a series of 150 cases, fifty in each group of comparative degree of pathology, who were treated by cauterization, coagulation and conization respectively. Those treated with cauterization were cured more quickly and there was no complication in this group. Nabothian cysts and cervical erosions were best treated by cauterization. Moderate stenosis of the cervical canal occurred in six patients treated by coagulation. Acute inflammation of the tubes and ovaries developed in four patients treated by coagulation, and in three treated by conization. Six patients treated by coagulation had a subsequent period of amenorrhea lasting from three to fourteen months. He concluded that cauterization is superior to electrocoagulation and conization. We heartily concur with him in this conclusion.

*Leucoplakia.* With a wire loop as the active electrode, the patch with a small circle of its surrounding normal tissue is removed, using a fast cutting current, as for Hyams' conization. The tissue removed is examined microscopically.

*Stricture and Stenosis.* Prevention is better than cure, and since many cases are due to treatment, one of the important steps is to become experienced with the above methods before undertaking their use. Another point is to follow up cases, especially where canal coagulation, conization or intra-uterine radium treatment has been done, once a month for three to six months, testing the patency and caliber of

the canal. When the patient is seen with stricture or stenosis already present, great improvement is often possible by gentle dilation with Hegar's metal dilators. This can easily be done in the office. (Fig. 14.)

The anterior lip of the cervix is grasped with a tenaculum, the canal cleansed, anesthetized with 35 per cent cocaine solution applied to beyond the internal os. Dilation is gently and gradually started with as small a dilator as is necessary, increasing gradually up to Hegar's dilators No. 12 or 13. It may require several treatments before this size is reached. For strictures we dilate once weekly, and for stenosis once a month just preceding the period. If the stricture completely occludes the canal and cannot be overcome, it passes beyond the realm of office treatment. In acquired stenosis, the relief of dysmenorrhea is immediate and considerable. Usually if the dilation is done before three successive periods, no further treatment is necessary.

I have used this method of cervical dilation immediately preceding the menstrual period for severe primary dysmenorrhea where the internal os is very tight, often accompanied with an acute ante-flexion. There are a surprising number of cases which respond remarkably well after three such monthly treatments. The procedure is so simple that it is well worth trying.

#### SUMMARY

This paper discusses the office treatment of the following cervical lesions: erosions, nonspecific endocervicitis, lacerations complicated by eversion and/or erosion, cysts, polyps, stricture, stenosis, leucoplakia, endometriosis, varicosities, and "strawberry cervix." Cervical anatomy and pathology are reviewed briefly. Accepted methods of office treatment of these lesions are discussed.

#### CONCLUSIONS

The cervix is the most common source of pathology in the pelvis. Twenty per cent of

virgins and nulliparae and 70 to 80 per cent of multiparae are affected.

Cervical pathology is responsible for a considerable amount of discomfort and invalidism. It may cause postoperative and postpartum infections, and is the most important predisposing cause of carcinoma of the cervix.

Physical examination of a woman is incomplete without a pelvic examination including careful inspection of the cervix.

Postnatal care should always include inspection of the cervix, and the period of observation should be six months rather than six weeks.

Topical application as a cure for most cases of cervicitis is inadequate and should be restricted only to that small group where the more effective electrosurgical methods are contraindicated.

Dickinson's method of cauterization with the nasal tip cautery marks the greatest improvement in treatment. It is the simplest in application, gives the best results in the largest number of cases, with a negligible percentage of complications resulting from the treatment.

Electrocoagulation and Hyam's conization are good methods, the latter especially being helpful for the badly infected endocervix with the small os. There is a higher percentage of complications following these methods, even in the hands of experts.

Acute infection of the cervix or other pelvic organs is a contraindication to electrosurgery. Pregnancy is no contraindication, but gentleness should be particularly stressed in this group.

Cervical stricture and stenosis, especially the latter, can usually be overcome by gradual dilation with Hegar's dilators.

The large body of physicians throughout the country could easily acquire the knowledge and armamentarium which would enable them to increase and enlarge their usefulness in the office treatment of cervical pathology.

#### REFERENCES

1. HOLDEN, F. C. Treatment of cervicitis, particularly by the cautery and operation. *Am. J. Obst. & Gynec.*, 16: 624, 1928.

2. WOLLNER, A. Etiology and treatment of endocervicitis and cervical erosions. *Am. J. Obst. & Gynec.*, 37: 947, 1939.
3. MATTHEWS, H. B. Pathology and office treatment of chronic endocervicitis. *Am. J. Surg.*, 36: 233, 1937.
4. FALK, H. C. Practical Clinical Gynecology. New York, 1938. American Journal of Surgery.
5. ROBLEE, M. A. On the etiology of cervicitis. *Am. J. Obst. & Gynec.*, 35: 1039, 1938.
6. DICKINSON, R. L. Rebellious cervicitis from cysts high in the canal. *Am. J. Obst. & Gynec.*, 16: 11, 1928.
7. LEIP, F., and OTTO, K. Cervical carcinoma which arose on twelve year old leukoplakia. *Zentralbl. f. Gynäk.*, 61: 242, 1937.
8. POLAK, J. O. Gyn. and Obst. Monographs. New York, 1922. Appleton.
9. FULKERSON, L. Endocervicitis: a clinical study of 1038 cases. *Am. J. Obst. & Gynec.*, 12: 374, 1926.
10. KLEEGMAN, S. J. Sterility. *Am. J. Surg.*, 33: 392, 1936.
11. HÜHNER, M. Sterility in the Male and Female and its Treatment. Rebraun and Co., 1913.
12. MOENCH, L. M. Relationship of chronic endocervicitis to focal infection with special reference to chronic arthritis. *J. Lab. & Clin. Med.*, 9: 289, 1924.
13. CURTIS, A. L. Gynecological Diagnosis. Philadelphia, 1929. Saunders.
14. SCHILLER, W. Early diagnosis of carcinoma of the female generative organs. *Wien. klin. Wchnschr.*, 49: 1533, 1931.
15. GEINSDORF, W. Observations on the colposcope. Year Book of Obst. and Gynec., 1939.
16. DAVIES, T. A. Primary Syphilis in the Female. New York, 1931. Oxford University Press.
17. DE LEE, J. B. Obstetrics. Philadelphia, Saunders.
18. GOODALL, J. R., and POWER, R. M. H. Pathology and treatment of inflammatory diseases of the cervix. *Am. J. Obst. & Gynec.*, 33: 1050, 1937.
19. HOLDEN, F. C. Lesions of the Cervix. In Curtis, Obstetrics and Gynecology, 3: 535. Philadelphia, Saunders.
20. FILLER, W., et al. Negatol in the treatment of cervicitis and trichomonas vaginalis vaginitis. In press.
21. ROSS, J. W. Chromic acid in the treatment of chronic infective endocervicitis. *Am. J. Obst. & Gynec.*, 33: 348, 1937.
22. SIREDEY, A., and BIGART, E. Recherches sur la leucorrhée. *Gynéc.*, 10: 202, 1905.
23. GREENHILL, J. P. Office Gynecology. Chicago, 1939. Year Book Publishers.
24. KENNEDY, W. T. Chronic endocervicitis. *Am. J. Obst. & Gynec.*, 1: 929, 1921.
25. HELVESTINE, F., JR., and FARMER, F. A. Infiltration of the cervix uteri with mercurochrome 220 soluble in the treatment of cervicitis and endocervicitis. *Am. J. Obst. & Gynec.*, 18: 68, 1929.
26. KRITSCHESKY, L. S., and WERBATUS, E. A new method of treatment of endocervicitis and erosion of the cervix with injections of solutions of ammonium silver salts. *Monatschr. f. Geburtsb. u. Gynäk.*, 101: 349, 1936.
27. HOLLENDER, A. R., and GRATTIOT, W. M. A non-operative procedure for the treatment of cervicitis and endometritis. *Am. J. Obst.*, 79: 523, 1919.
28. TOVEY, D. W. Copper ionization in the treatment of cervicitis. *New York State J. Med.*, 30: 887, 1930.
29. HUNNER, G. L. Treatment of leucorrhea with the actual cautery. *J. A. M. A.*, 46: 191, 1906.
30. DICKINSON, R. L. Endocervicitis and eversion and the nasal tip cautery. *Am. J. Obst. & Gynec.*, 2: 600, 1921.
31. GOLDBLATT, S. Gonorrhea in the female: a study of 3,838 cases with special reference to electro-surgical treatment of gonorrheal endocervicitis. *Venereal Disease Information*, 157, June, 1939.
32. GOODALL, J. R., and WISEMAN, M. Cervical infections in the puerperium. *Am. J. Obst. & Gynec.*, 16: 339, 1928.
33. ENDE, F. M. Coagulation diathermy in cervicitis using a new electrode with an account of its results in 200 cases. *Am. J. Obst. & Gynec.*, 18: 72, 1929.
34. CHERRY, T. H. Bipolar Coagulation of Chronic Endocervicitis. Chicago, H. G. Fisher.
35. BARRETT, R. L. Puerperal cervix. *Am. J. Surg.*, 33: 541, 1936.
36. HYAMS, M. N. Conization of the uterine cervix. *Am. J. Obst. & Gynec.*, 25: 653, 1933.
37. STURMDORFF, A. Gyno-Plastic Technology. Philadelphia, Davis.
38. JACOBY, A. A comparison of the end results of treatment of endocervicitis by electrophysical methods: cautery, coagulation and conization. *Am. J. Obst. & Gynec.*, 36: 656, 1938.



# THE IMPORTANCE AND METHODS OF SEMEN EXAMINATION IN CASES OF STERILITY

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THE importance of the male rôle in infertile marriages is becoming more and more evident. In part this is due to our better understanding of disturbances of fertility in general, and in part to the more accurate semen appraisal which can be carried out today. It is not many years ago that the male was blamed for an infertile marriage in not more than 10 per cent of all cases, and a semen examination was often not made at all, or at most a glance was given the semen under the microscope; if motile sperms in fair numbers were present, the man was absolved from any blame for the childless marriage. In fairness to the man it must, however, be admitted that if for one reason or another, not apparent to the examiner at the time, the sperms were not motile the patient was often entirely erroneously considered sterile. We know today that a cursory examination of the semen is entirely inadequate and that a man may have many actively motile sperms in his semen and still be infertile. In such cases, however, this infertility can only be determined by a very careful detailed analysis. With such an analysis many "obscure" cases of infertility clear up immediately. I, personally, feel that infertile marriages are as often due to the male as to the female.

For years I have been stressing a 50 per cent male-50 per cent female basis for sterility, and hope to see this recognized at a date not too far off. Already the previous 10 per cent of the cases of sterility ascribed to the male has generally been advanced to 25 per cent, and many other men even believe 40 per cent to be nearer the truth. Plain logic would speak for an equal distribution of the blame in infertile unions, but we also have empirical evidence in the case of animal breeders whose knowledge

human medicine neglected, perhaps because man considers himself such a superior animal. It is probably this reason, too, and the male ego which has long prevented the recognition of the male rôle in abortions, a fact well known to animal breeders for a long time.<sup>1,2</sup>

In dealing with human infertility we must first of all be careful to mean what we say. The term sterility is altogether too often used to mean lowered fertility and not sterility. The latter is the state of complete inability to impregnate or conceive, and usually due to such gross factors as absence of the vagina, atrophic testes or ovaries, closed vasa deferentia or Fallopian tubes, etc. Thus problems of diagnosis are generally not created by these cases. It is the disturbance of fertility of lesser degree which creates the diagnostic difficulties. In such cases it is not unusual to see couples who consider themselves sterile, when as a matter of fact the woman conceives from time to time, but aborts spontaneously soon thereafter. These early abortions are then usually interpreted simply as delayed menstrual periods. It is now a well established fact that most spontaneous abortions are due to abnormalities of the zygote. It is often inadvisable, therefore, unless one knows the complete status of both prospective parents, to try every measure possible to save what may turn out to be an abnormal child. This fact I have stressed repeatedly.<sup>3</sup>

Each infertile couple is an individual problem. No man or woman can be judged alone, but only in relation to his or her sexual partner. If we consider the ideal fertility of an individual as 10 (an ideal not present in actual life, especially in more highly civilized countries), then the combined fertility of two such individuals

would be 10 times 10 or 100 per cent. My experience has shown me that clinical sterility is present when the combined

family history and whether or not husband and wife were nine months babies. (Veterinarians have shown that under- and over-

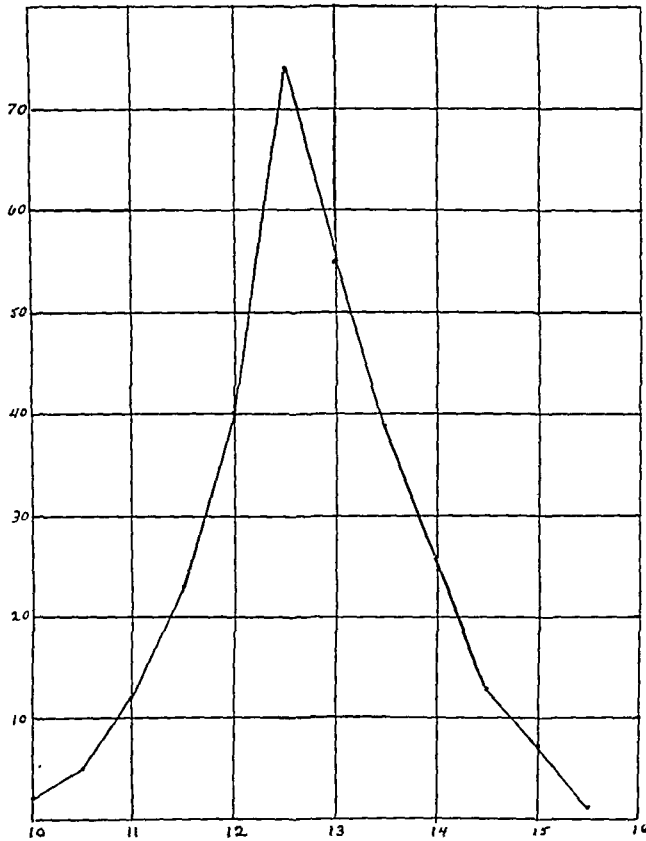


FIG. 1. A quite symmetrical graph of a normally fertile man with good seminal cytology. Coefficient of variability  $7.825 \pm .215$ . This graph, like Figures 2 and 3, was made up of the values obtained by measuring 300 sperm heads at a magnification of 3000 diameters in 0.5 mm. The values on the x ordinate are millimeters, those on the y ordinate indicate the observed number of sperm heads of this particular size.

fertility sinks below 60 per cent. Sixty, however, can be made up of various figures (9 times 7, 8 times 8, etc.) and thus one sexual partner can within reasonable limits make up for the infertility of the other. In this way it is easy to explain the formerly puzzling cases of infertile unions which broke up, but later when each partner married some one else, both couples had children born to them. Every sterile couple requires investigation both as individuals and in relation to one another.

The examination must start with a painstaking anamnesis which includes the

carried offspring later on are often of poor fertility.) General and special diseases and operations must be asked about, as well as dietary and sexual habits recorded. The breeding record of the couple must be very closely examined, since the birth of a child does not in any manner indicate a satisfactory evidence of fertility, since repetition of intercourse by the same two partners may eventually lead to pregnancy, even if the fertility is rather low.<sup>4</sup>

General and special physical examinations must follow the taking of the history. That endocrine disturbances and abnormal

basal metabolism reactions are very important need not be stressed here, since this is so well known.

ously on the spermatozoa and kills all of them, probably in less than twenty-four hours, and certainly in forty-eight hours.

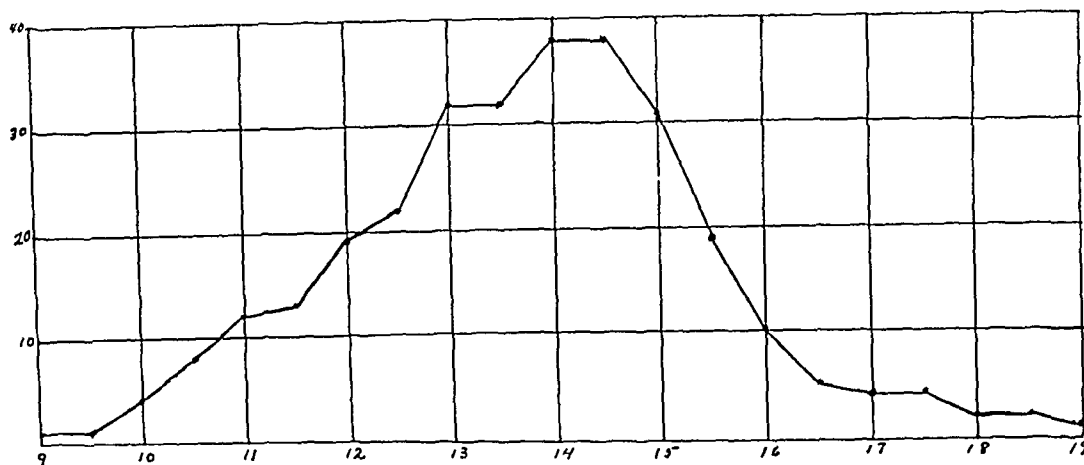


FIG. 2. Graph of a sterile man with poor seminal cytology. Coefficient of variability  $12.900 \pm .355$ .

In the case of the male the genitals must be examined for abnormalities. The size of the testes, within reasonable limits, is not so important here as the consistency of the gonads. Soft testes usually indicate disturbed spermatogenesis, but unfortunately the reverse is not true. The prostate and seminal vesicles must also be palpated for determination of size, congestion, inflammation, tenderness, etc.

Following this an examination of the semen is carried out. The best way to obtain this is as a friction specimen produced in the office. For one reason or another it is not always possible to secure such a specimen. Then a specimen as fresh as possible should be obtained, either by intercourse and withdrawal and ejaculation into a clean glass container, or with a condom, providing the semen is taken out of the condom immediately. Preferably this is done by holding up the condom and snipping the closed end at the bottom with a sharp pair of scissors. In this way the semen will come into contact with the minimum amount of rubber.

The semen should then be delivered as soon as possible to the office, being kept cool in the interval at the open window except in extremely cold weather. Too often the semen is kept warm, but we know today that even body temperature acts deleteri-

This was a paradoxical fact as long as the sperms were considered to be stored in the seminal vesicles, but we know today that the sperms are stored in the tail of the epididymis where they are at a lower than body temperature.<sup>5</sup>

Because of the deleterious effect of body temperature it is not good to leave the tied or twisted condom in the vagina to be brought to the office by the woman. Here a doubly deleterious effect—from the condom and the body heat—is acting. The method of taking semen from a seminal pool in the vagina after coitus is also not good, since, first of all, the presence of vaginal secretion and cells adds to the difficulty of proper semen examination, and if the examination is done immediately after coitus, no knowledge of the action of the vaginal secretion can be obtained. If examination is done, as is usual, after an hour or so, the sperms which are normal should already be up in the cervix and beyond reach of the examiner. Furthermore, we can be certain today that such a condition as sexual incompatibility of a man and a woman does not exist. All the known races of mankind are fertile with one another and produce fertile offspring, so that it is the height of illogic to predicate sexual incompatibility between two sexual partners who are most often of the

same race. This hypothesis of sexual incompatibility was evolved for cases not explainable with the former state of our knowledge.

ally of little use to test the seminal hydrogen ion concentration. Unless this is done with very definite precautions the results

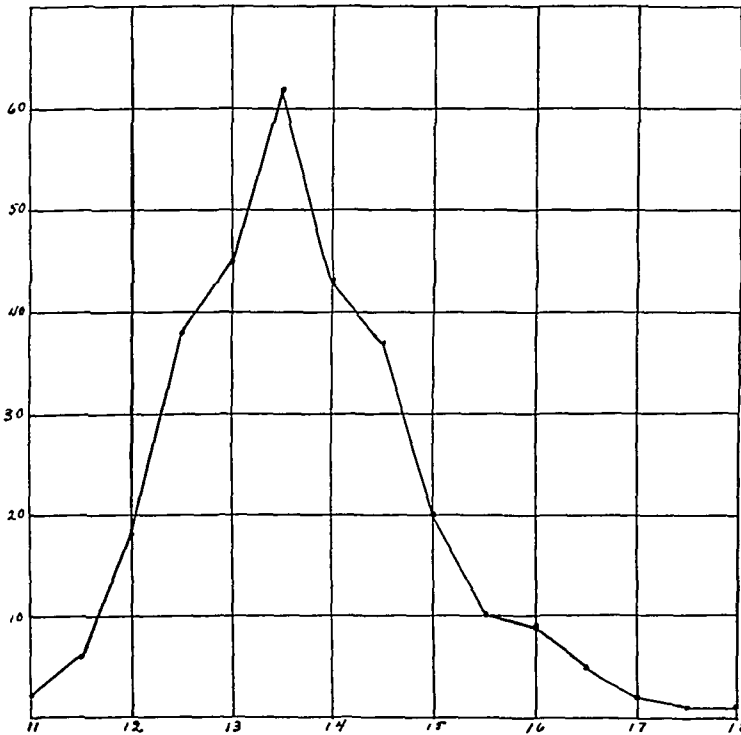


FIG. 3. Graph of a man of very low fertility (practically sterile), with good seminal cytology and a coefficient of variability of only  $8.521 \pm .239$ . The skewness factor, however, was 5.62 times the probable error.

After the semen reaches the office it should be examined for quantity, color, turbidity and viscosity. Lessened quantity may mean diminished action of the secondary sex glands, either congenital or acquired, due to disease, endocrine imbalance, age, etc. In normal cases, frequency of intercourse will cause lessened amounts of ejaculated semen. Color and turbidity of the semen will be influenced by blood and pus or diminished prostatic secretion; the latter will often decrease turbidity and viscosity. Increasing age leads sometimes to a gritty semen due to prostatic concretions. Increased viscosity of the semen is due also to diminished amounts of seminal production, due to diminished sex gland activity or frequency of intercourse. Unless markedly increased, viscosity does not have much effect on the fertilizing power of the semen. It is gener-

ally valueless, and furthermore, the semen has such a powerful buffer reaction that the hydrogen ion concentration automatically takes care of itself.

A slide of the semen is then made and the number and motility of the spermatozoa observed. Also the presence or absence of blood, pus, and extraneous substances is observed. Since this has been taken up in a previous article in this Journal,<sup>6</sup> I will not go into it here. I only wish to stress that the semen should be observed for five to six hours in every case.

While the fresh semen is being observed, smears of the semen are made on slides, using the technique of making blood smears. These smears should be as even and as thin as possible, except that if very few sperms are present, thicker smears may be used to obviate the extremely tedious labor of counting a sufficient number of cells.

This is, however, but the choosing of the lesser of two evils, as the smears naturally will not be so clear as thinner ones.

The smears are then quickly dried by an air current and passed through the flame just enough to fix them, that is, they should feel only warm to the back of the hand. Depending on the amount of mucus present, the slides are immersed in a 1 per cent chlorazene solution for 15 seconds to several minutes, then washed carefully with distilled water and 95 per cent alcohol. This latter is necessary to prevent precipitation of the alcohol-soluble stain. This stain consists of:

	Parts
Ziehl-Neelsen's carbolfuchsin.....	50
Eosin (Grübler's bluish alcohol-soluble).....	25
Ethyl alcohol, 95 per cent.....	25

This stain is made up and filtered. When a slide is to be stained, some of the stain is poured into a small dish and carbolfuchsin is added, a few drops at a time, until a metallic film forms on the surface of the solution. The solution is then filtered and used. It is, however, possible to use the stock solution directly if care is used to avoid precipitates by refiltering when necessary.

The stain is spread evenly over the whole slide in adequate amounts to prevent drying and precipitation, and left on three to five minutes. It is then poured off, the slide washed in distilled water, and stained a few seconds with Loeffler's methylene blue diluted 1:4 with distilled water. The slide is then washed again, dried, and examined under the microscope, using an oil immersion lens and a 10× ocular. If the slide is for morphologic studies only, it is well to have a good blue counterstain. For biometrical purposes, however, it is easier on the eyes to keep down the blue color.

It has been repeatedly asserted by some men that my methods of preparing the slides cause artificial sperm changes. This had been checked by me at the very beginning of my investigations and found to be untrue. Since then it has been checked again and again, always with the same

results. Furthermore, of the dozens of staining methods which I have investigated, the one described is by far the best, at least in my hands, and I have yet to see slides made by others which are superior to mine. One might also say that if sperm changes are produced by the handling of the smears which allow of a determination of the fertility of the individual, so much the better.

In the morphologic studies the various sperm forms are tabulated as normal, body changes, and head changes. It is the latter which offer the best index of fertility. Head changes are classified as small, large, narrow, tapering, round, heads with overdeveloped end knobs, solid staining and amorphous head forms. (My plates of the various sperm abnormalities have appeared a number of times so that it does not seem necessary to republish them here again.<sup>3a,3c,7</sup>)

After one has gotten a general impression of the slide and the average size of the sperm heads in the particular case (they vary somewhat in mean size, even in normal cases), it is not difficult to distinguish between a very large and a very small head, or to pick out long tapering or narrow heads. That, however, is not the crux of the matter. It is evident that there will be gradations of every conceivable type in the sperm head abnormalities, and it takes a large amount of experience to know where to draw the line between normal and abnormal sperm forms. Unless the examiner possesses such experience, which can only be obtained by intensive practical work, his results will not only be unreliable but often entirely erroneous. In such cases even a cursory semen examination would be preferable, as at least it would not lead to complete reversal of the true facts in the opinion of the man or men treating the particular infertile couple.

As an illustration of my point, I may cite a case in which the semen of a man was said to contain very many extremely motile sperms and no abnormal heads (normal—up to 20 per cent abnormal head



forms). Yet the wife, who had been found normal, never conceived. The conclusion drawn by the physician, therefore, was that sperm cytology did not allow of a determination of the fertility of an individual. On account of the importance of the questions involved, I was naturally very much interested. In 1926 I had introduced the detailed semen examination to the medical profession. Since then all my efforts to disprove the assumption that sperm characteristics allow of a determination of the fertility of the individual have failed. On the contrary, a vast amount of evidence has accumulated to support the value of the detailed semen examination. In 1926 I tentatively set 20 per cent abnormal head forms as the dividing line between normal and disturbed fertility. Between 20 to 25 per cent abnormal head forms indicated diminished fertility, and abnormal head forms above 25 per cent usually meant at least clinical sterility within the reservations already mentioned pertaining to human relationships. I builded better than I knew at the time because experience has supported my original figures practically entirely. In all my cases, however, I had never seen a single one with less than 7 to 8 per cent abnormal head forms, and even these were few and far between; 10 to 15 per cent abnormal head forms represented the usual findings.

In view of these facts, I am extremely suspicious of sperm counts purporting to show no abnormal sperm heads or even 2 to 3 per cent of such changes. It was possible later to check the case and 26 per cent abnormal sperm heads were found. It was easy to understand why such a discrepancy was possible, since most of the sperm head abnormalities consisted of size differences, hard to evaluate at the magnification of 1000 diameters which is ordinarily employed. The biometrics corroborated my morphologic count since the coefficient of variability was very high.

Such a case shows the importance of thorough versing in sperm changes. This is just as much a question of morphology as is tissue diagnosis. I frequently receive requests for descriptions of the technique of my method of sperm examination, because some one wants to try it on a case, or have his nurse or secretary do it. This simply cannot be done. These same men without proper training certainly would never attempt to diagnose an early carcinoma of the cervix, or detail their nurse or secretary to do it. Yet on the results of the semen examination depend the further handling of the case and at times the question of operating on the wife.

It is evident also that a simple summation of the number of abnormal sperm heads does not give the complete picture. Different types of sperm head changes have varying significance and the same types of cells in different specimens do not always have the same importance—narrow and tapering sperm heads indicate the greatest disturbance of spermatogenesis, and such disturbance is more or less directly proportional to the number and length of the sperm heads and their narrowness. Thus a sperm head count may show 20 per cent or less abnormal sperm heads and still mean infertility if these narrow and tapering sperm heads total more than 7 to 8 per cent. Again a semen may show the same sperm head count after treatment as before and still be improved, as shown by a shortening of the narrow and tapering sperm heads. Round sperm heads are not of great significance, but become even less important when in this particular semen most of the sperm heads show a tendency toward roundness.

In evaluating a sperm count all these various factors have to be taken into consideration. If the sperm head abnormalities are very numerous one can stop there, since the infertility of the man has been determined. Usually, also, a poor morphologic picture is associated with a poor biometrical result, but this is not necessarily so. Therefore a normal sperm head

count does not absolve the man from all blame for the infertile marriage because many of the sperm head size differences may escape notice in the ordinary morphologic examination, but will be revealed by the biometrical methods.<sup>8</sup>

Biometrics are carried out either by filomicrometer measurements (a very tedious procedure), or preferably by projecting the sperm head images onto a very glossy piece of paper (pinwheel paper) and measuring the length of 300 to 500 sperm heads in 0.5 mm. by means of set screw calipers. A graph is then constructed from these values. The functions of the graphs are determined, and if the coefficient of variability is above 11 or 11.5, disturbed fertility is usually present. It is unfortunately true that even normal morphology and normal simple biometrics do not always indicate fertility. The lopsidedness of the graph obtained must at times also be taken into consideration, since such skewness can only be produced by an abnormal number of small or large sperm heads. If such calculated skewness exceeds four times the probability of error it becomes significant. Such skewness was the only disturbance we could find in a few of our cases, yet the clinical history and course completely verified our calculated results. (Figs. 1, 2, 3.)

While the value of the described detailed sperm examination has been accepted by most men, some have voiced the objections that the seminal picture is not constant, that it is not important whether 85 per cent or 60 per cent of the sperm heads are normal (in cases with 15 or 40 per cent abnormal sperm heads) and that the difference between 20 and 25 per cent (normal limit and sterility) is too small to be considered seriously as a factor in sterility.

These objections are, however, not valid, and are based in part on wrong premises. First of all, except in disease and with age, the seminal picture does remain constant as far as the morphology and biometrics is concerned. This was the first point I had had to determine before I could even

attempt to correlate seminal cytograms and fertility. It is true that frequent coitus reduces the number of the sperms, but the morphology always remains constant, except for a slight increase in immature sperm cells, cytoplasmic drops, and an occasional spermatid. Sexual abstinence for some time may increase the number of abnormal sperm forms in the first ejaculate (not after that), since the old dying and degenerated sperms gradually find their way into the seminal vesicles where most of them remain until ejaculation takes place. The constancy of the seminal picture in the same man within reasonable limits of time (that is, avoiding the inevitable onset of increasing abnormalities with age) has again and again been checked by me. Thus a three months' abstinence and daily intercourse for several weeks did not change the seminal morphology or biometrics.

As far as the second objection is concerned, namely that "it is unimportant whether 15 or 40 per cent of the sperm heads are abnormal as long as the other cells are normal," this shows a complete lack of understanding for the basic principles on which the method of sperm examination is based.

It is axiomatic in nature that the crop is dependent on the soil. With a good soil a numerically good crop is obtained, and with pure strains the fruit borne will all be more or less of the same shape and size with certain normal variations. With a poorer soil a poorer crop will be obtained and the shape and size differences will increase. After studying some particular pure strain crop, say Victoria peas, the percentage of the aberrations of size and shape from the normal can be fixed, and it will be found that if the soil is very poor a stage will be reached where none of the peas are fully developed, at least internally, so that even those that look normal to the eye, when planted, will not germinate. By tabulating the variations of size and shape it will be possible to predict this lack of germination in advance. In other words, the externally visible abnormalities are the

recognizable indicator of the degree of disturbance present in the whole crop. In the same way the sperms are the crop of the seminal tubules and the visible abnormalities are simply used in the same way as an indicator. Experience has shown me that when more than 20 per cent of the sperm heads are visibly altered all of the sperms have been affected to some greater or lesser degree, depending on the number of visible abnormalities above 20 per cent and the type of changes. Thus 40 per cent abnormal sperm head forms now means 40 per cent visibly abnormal sperms and 60 per cent also abnormal sperms (here and there one—perhaps one in a thousand—may be normal) but not recognizable with our crude microscopic equipment.

As far as the difference between 20 and 25 per cent goes, this is a difference of 25 per cent. No one, I believe, will have the temerity to deny, for instance, that a 25 per cent difference of thyroid function is insignificant.

Aside from the spermatozoa, semen also contains cytoplasmic drops and cells from the genital tract of the male—urethra, prostate, testicular tubules, etc. Normally the number of these cell forms is not large. But they are important and significant. I have, however, already discussed them in detail and refer the interested reader to the preceding article.<sup>6</sup>

Summing up all the findings discussed so far, then, we see that a number of different seminal pictures are possible. These can be epitomized as follows:

A. Normal cases: semen ejaculate grossly normal, totaling 3 or more c.c. with 60 or more millions of actively motile sperms per c.c. (There is, however, a wide variation of the normal limits both as to the amount of semen ejaculated and the number of sperms per c.c., as pointed out previously.<sup>6</sup>) Very small semen specimens of 0.5 c.c. or less are, however, usually abnormal. There should be 20 per cent or less abnormal sperm head forms with less than 7 or 8 per cent combined narrow and tapering head forms. These should not be of the

extreme variety. Double and unripe forms should not exceed 2 or 3 per cent each. The cytoplasmic drops may reach 4 or 5 per cent and cells of spermatogenesis should total not more than 0.5 to 1 per cent.

The biometric results should show a coefficient of variation of not more than 11.0 to, at the most, 11.5. Skewness should not be significant.

B. Sexual overloading in a normal individual, and also temporary disturbances, may and do lead to decreasing numbers of spermatozoa and increasing numbers of cytoplasmic drops, coiled and immature sperms and spermatids, though the latter will still be relatively rare.

C. Sexual hypoplasia of a mild degree will also give a picture similar to the preceding, but later rechecking will allow of a differential diagnosis. In the severer degrees of hypoplasia, of course, more marked abnormalities are seen, down to an ejaculate of only a few c.mm. containing practically no sperm cells and only some testicular spermatogenic cells.

D. Testicular degeneration in a mild chronic form also shows pictures similar to B and C, but here many sperm head abnormalities, especially many long and narrow and tapering sperm heads are seen. Often indeed a complete museum of sperm abnormalities is present. Severer degeneration will show fewer and fewer sperms, more abnormal forms, and more degenerated spermatids, up to a certain point, after which the seminal ejaculate will be small, show few, mainly abnormal, sperms, and practically no cytoplasmic drops or spermatids since spermatogenesis is at a very low ebb. In acute degeneration the whole testicular tubular cell lining may be extruded, often in sheets, depending on the severity of the condition. Sperms will be absent. Later on neither sperms nor cells of spermatogenic origin will be found. This picture is identical with that of bilateral vas obstruction. Testicular puncture will show sperms in the last case, but not in the first.

E. Testicular regeneration—after long continued severe sexual overloading or

following treatment—will give a picture very similar to c. Cytoplasmic drops may equal the number of the sperms and up to 20 per cent of the cells seen may be spermatids. The increasing number of sperms will, however, immediately show the true condition present.

Thus a careful semen evaluation forms a criterion not only of the present state of the patient's fertility, but also to a certain extent gives a hint as to the prognosis. The latter, however, must always be very guarded. Every case is a problem in itself and no guarantees can be given even in apparently identical cases because of our still very great ignorance of endocrinologic disturbances.

*Treatment.* Since general good health is intimately associated with fertility, good common sense in living is of vital importance. Coitus should be reduced to a feasible minimum. Thyroid is advisable in all cases where the basal metabolism is even slightly low (and it has been low in the majority of my cases). Vitamin E, essential to growing cells, should be given in doses of about a dram a day. In addition, gonadotropic hormones, that is, the follicle-stimulating hormone of the anterior pituitary, should be given. Through the courtesy of Parke, Davis and Company and of E. R. Squibb and Sons I have used antuitrin and gamone extensively with some very good but entirely unpredictable results. Although I have used these drugs, especially antuitrin, for several years, It is still too early for me to make any didactic statements about these products. I will say, however, that were it not for the patients' patience giving out, usually in the short time of a few months, very much better results could have been achieved. Most of my patients have shown at least some improvement. Some have reached a perfectly normal state and have had children, provided the wife was normal. Other cases, however, have been complete failures. Frequently, however, if after three months' treatment the patient's wife was not yet pregnant the treatment would be discon-

tinued in disgust. Often the patient would expect a condition he had had for ten or more years to be cleared up in three or four weeks. No doubt with our steadily increasing knowledge of the endocrines better results will be obtained in the future in cases of spermatogenic disturbances.

There remains only one other question to be discussed and that is the question of operation in men with obstruction of both vasa deferentia. An operation connecting the vas deferens beyond the obstruction to the head of the epididymis is neither difficult nor dangerous, but rather patience-trying on account of the small caliber of the vas. The results of such an operation, even if patency of the vas should remain established, are rather questionable because the sperms only mature as they pass on from the head of the epididymis to the tail; thus most of the sperms after a vasoepididymostomy will be immature. The same objection can be raised against the attempt to produce pregnancy by injecting into the cervical canal sperms obtained by testicular puncture. Besides, only very few, slightly motile sperms can be thus obtained. However, the literature does contain some cases in which such measures resulted in pregnancy.

#### CONCLUSIONS

Summarizing the present article and also the one which appeared in the March issue of this Journal the following conclusions seem warranted:

1. Every infertile couple presents an individual problem which can only be assayed if both partners are properly investigated since the fecundity of the couple depends on the relative fertility of one partner to another.

2. The fertility of the man depends more on the qualitative than on the quantitative production of spermatozoa.

3. Motility of the spermatozoa must be evaluated very carefully as there are many, almost imponderable, sources of error which may lead to entirely erroneous conclusions.

4. The informative value of the detailed semen examination seems to be well established today. Apparently contradictory reports so far have been shown to be due to improper interpretation of the seminal findings. This but emphasizes the fact that the proper recognition of the various abnormalities in the seminal cytogram is a morphologic problem which requires detailed training and experience. It is generally true that sperm head abnormalities totaling more than 20 per cent indicate at least some disturbance of fertility. There are, however, exceptions to this rule and a simple summation of the sperm head abnormalities does not show the whole picture. Aside from the spermatozoa themselves the other cells of spermatogenesis are important for the complete evaluation of any semen specimen.

5. As a rule sperm morphology and biometrics run parallel, but this is not necessarily so. Usually a graph with a coefficient of variability above 11.0 to 11.5 indicates a disturbance of fertility, but in some cases both the seminal cytogram and the simple functions of the graph may be normal while a disturbance of fertility is indicated by a marked skewness of the graph.

My experience over the years has shown me that if all the points mentioned are given due consideration, unexplained cases of sterile marriages will be decidedly rare. However, it must not be forgotten that repetition of intercourse may lead to conception even in cases with low fertility. The occurrence of such conception may be

seen at any time and is entirely unpredictable. A recognition of this fact will explain some otherwise apparently paradoxical cases. The rôle of the male in abortions must also be remembered.

Therapy of disturbed spermatogenesis is still in its infancy. In my hands the best results were obtained with the follicle stimulating or spermatogenic factor of the anterior pituitary gonadotropic hormone.

#### REFERENCES\*

1. WILLIAMS, W. L. Significance of duration of pregnancy. *Cornell Vet.*, 17: 331, 1927.
2. CONKLIN, R. L. Relation of sexual health of domestic cock to fertility and hatchability of eggs. *Cornell Vet.*, 19: 25, 1929.
- 3a. MOENCH, G. L. A consideration of some of the aspects of sterility. *Am. J. Obst. & Gynec.*, 13: 334, 1927.
- 3b. MOENCH, G. L. A consideration of some of the aspects of sterility. *Am. J. Obst. & Gynec.*, 32: 406, 1936.
- 3c. MOENCH, G. L. Studien zur Fertilität. Stuttgart, 1931. Ferdinand Enke.
4. MOENCH, G. L. Determination of breeding record in couples with distributed fertility. *Am. J. Obst. & Gynec.*, 19: 77, 1930.
5. MOENCH, G. L. Longevity of human spermatozoa. *Am. J. Obst. & Gynec.*, 38: 153, 1939.
6. MOENCH, G. L. Relation of certain seminal findings to fertility. *Am. J. Surg.*, 47: 586, 1940.
- 7a. MOENCH, G. L. Report on sperm examinations in obscure cases of sterility. *M. J. & Rec.*, July 20, 1927.
- 7b. MOENCH, G. L. Zur Frage d. menschl. Fertilität. *Zentralbl. f. Gynäk.*, 43: 2730, 1927.
- 7c. MOENCH, G. L. Some phases of the problem of sterility. *Med. Herald & Physiotherap.*, 47: 61, 1928.
- 7d. MOENCH, G. L. Sperm morphology in relation to fertility. *Am. J. Obst. & Gynec.*, 22: 199, 1931.
8. MOENCH, G. L. Biometric studies of head lengths of human spermatozoa. *J. Lab. & Clin. Med.*, 17: 297, 1932.

\* For a more complete bibliography see the March, 1940 number of this Journal, page 586.<sup>6</sup>



# CHRONIC SUBINVOLUTION, CHRONIC METRITIS AND HYPERTROPHY OF THE UTERUS\*

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CHRONIC subinvolution was accurately described by Fletcher Shaw as early as 1914. Before this the term fibrosis was applied to many benignly enlarged uteri. In spite of this, modern textbooks discussed the condition very vaguely, if at all. In 1918, the writer confirmed the work of Shaw, but the subject, important as it is, received very little attention in the literature. As late as December, 1938, the author reviewed the subject before the Baltimore Gynecological Society, and the discussion that arose pointed out clearly that comparatively little was known generally about this rather common gynecologic lesion. To give an idea of the frequency of the condition, one needs only to quote routine laboratory figures. Since 1919 we have routinely stained every uterine section with hematoxylin and eosin, and orcein Van Gieson, classifying them as normal, chronic subinvolution, chronic metritis, hypertrophy and diffuse adenomyosis. Since the return of Gynecology to Obstetrics at Washington University School of Medicine in 1929, this routine was continued and the following figures give one an idea of the frequency with which these various lesions were met as compared to the frequency of myomata.

Number of specimens from July 1, 1929 to July 1, 1939.....		11,483
Chronic metritis.....	262	
Adenomyosis of uterus.....	586	
Chronic subinvolution.....	583	
Hypertrophy of uterus.....	9	
Myoma of uterus.....	1,632	

It will be noted that clear-cut hypertrophy occurred only nine times. These lesions are definitely forerunners of diffuse adenomyosis, the invasions of the muscula-

ture taking place after the presence of hyperplasia of the endometrium and hypertrophy of the wall.

## CHRONIC SUBINVOLUTION

Although the characteristic features of the changes of distribution of elastic tissue in a parous uterus have been described for some time by numerous writers, the clinical diagnosis of chronic subinvolution was not definitely suggested until the work of Fletcher Shaw as late as 1917. Before this time the term "chronic metritis" was often applied to a definitely enlarged uterus which was associated with retroversion, pain and hemorrhage. The term "chronic metritis," naturally, suggests inflammation, and in chronic inflammatory processes there is frequently an increase of connective tissue present. Thus the term "fibrosis uteri" developed and was freely applied to all symmetrically enlarged uteri in the absence of newgrowth. Fletcher Shaw pointed out that these enlarged uteri were most commonly due to changes which were characteristic of subinvolution. He described the pathologic changes of a uterus affected with chronic subinvolution, chronic metritis and also gave us a clear picture of hypertrophy of the uterus. In this study he pointed out that these three conditions could exist as separate entities, but the picture was often confused because of the overlapping of these conditions, that is to say, one or more of these lesions could be present in the same uterus. In 1918, the writer confirmed Fletcher Shaw's work and pointed out clearly that subinvolution was the most frequent lesion found in these enlarged uteri, but that the picture was sometimes difficult to describe because of

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the distinct overlapping of these above mentioned conditions.

Although the pathology of these benign lesions of the uterine wall has been well described, they have received comparatively little clinical attention, and I thought it might be interesting to discuss this subject again and compare our present findings with those of previous studies made a good many years ago.

The best descriptions of the constituents of the normal nulliparous uterus, pregnant uterus and the processes of involution as well as the changes due to subinvolution, in our opinion, are those of Fletcher Shaw. Although these descriptions were made in 1917, they have never been fully emphasized in our American textbooks on gynecology. As they have a definite practical bearing, I shall review these changes here, taking the liberty to quote freely from the previous work of Fletcher Shaw, which we confirmed several years ago.

*The Virgin Uterus.* Elastic tissue is found as the internal elastic membrane of the arteries. Fibrils of elastic tissue are also seen in the media and adventitia of the vessels. In the myometrium, elastic fibrils are located in between the muscle bundles, not conspicuously in the inner third, but more prominently in the subperitoneal area. There is no definite elastic interna of the veins. More elastic tissue, however, is present in the wall of the veins between the muscle tissue. Elastic tissue is very strikingly seen in the outer portion of the veins, and although not in the form of a membrane, it is sometimes referred to as the external elastic membrane.

*Uterus during Pregnancy.* All constituents of the uterus are increased. Muscle cells are enormously enlarged. There is an increase in fibrous and elastic tissue, the proportions of these structures being the same as in the normal nulliparous uterus. Marked enlargement of blood vessels occurs in order to take care of the growing organ and convey the necessary amount of blood to the fetus. All vessels are enlarged, but the most striking increase in size is

naturally seen in the subplacental site. In the involution of the puerperal uterus, the most marked atrophy known occurs. This process is often referred to as "atrophy acutissimus." The uterus, just after delivery, weighs approximately 1000 Gm. In three or four weeks, it is reduced in weight to from 4 to 6 ounces. This reduction in size is due chiefly to the diminution in size of the individual muscle cells by proteolytic processes within the cell wall. Some fatty degeneration is seen, but this is not conspicuous. There is also some total destruction of cells. Marked changes in the vessels take place, leading to their reduction in size or complete obliteration with marked degeneration of the walls of the arteries of the inner third of the uterine wall. Some vessels are closed either completely or partially by thrombi. There is a marked thickening of the intima of the arteries. The media of the vessel becomes markedly swollen and the internal elastic membrane undergoes vitreous degeneration (the term is suggested by Goodall). In this process the internal elastic membrane becomes greatly thickened and at various stages of this degeneration the staining properties with orcein or Weigert's and Van Gieson stain, vary. From the normal black-brown stain, it goes into a brick red, then a bright red, and finally, as absorption is about to take place, it stains only a faint yellow. The various stages of these degenerative changes can be seen in the same vessel.

The elastic fibers in the media go through a similar process. The adventitia also undergoes hyaline change as does the fibrous tissue of the media. The vessel now consists of a more or less conglomerate mass without any lumen or with a small opening remaining, through which the smaller new vessel subsequently develops. With the development of the new vessel in the patent area of the old, we see the new vessel surrounded by a degenerated structure, which if involution is complete, will be entirely absorbed. If during the process of involution, the vitreous degeneration stops and absorption does not take place, the

degenerated tissue regains the property of staining like normal elastic tissue. Thus, if this process is markedly hindered, we see numerous collars and pads around the newly formed arteries of the inner third of the uterine wall. In the larger arteries, the same process occurs as in the smaller ones, with the exception that the process consists chiefly of the development of a new internal elastic membrane and a new intima, the rest of the old wall remaining intact.

In the veins the walls become swollen due to marked hyalinization of the connective tissue with the compression of the muscle cells. The elastic tissue here also becomes very much swollen, but is so intermingled with the hyaline mass that it is not so distinctly seen as in the case of the arteries. If involution is complete, the hyaline mass is absorbed and new muscle cells develop. If the involution is not complete, the spaces between the muscle bundles of the vein contain the degenerated hyaline tissue, which regains the ability likewise to take the same stain as normal elastic tissue.

Elastic and fibrous tissue in between the walls of the muscle bundles undergoes changes similar to those described for the veins and arteries. This is especially true in the outer portion of the uterine wall. If these degenerated masses are not completely absorbed they regain the property of staining with orcein or Weigert's stain and appear as dark brown degenerated masses of tissue between the muscle bundles.

In the ordinary process of involution the absorption of the degenerating tissue is fairly complete, but there is usually sufficient lack of absorption of these structures around the arteries, in the veins and between the muscle bundles to differentiate a parous from a nulliparous uterus. If the absorption of these degenerating areas is checked, the characteristic picture of subinvolution comes into existence, namely, dark staining collars and pads around the arteries, unabsorbed dead elastic tissue in and about the veins, and similar tissue

between the muscle bundles of the outer third of the uterine wall.

#### PATHOLOGY OF HYPERTROPHY OF THE UTERUS

Hypertrophy of the uterus almost invariably is associated with a marked hyperplasia of the endometrium with a history of prolonged menorrhagia. The uterus is enlarged, chiefly due to a work hypertrophy, the musculature trying to rid the cavity of the excessive formation of the endometrium. Some authorities believe that the hypertrophic condition of the musculature is a primary thing, associated with the hyperplasia of the endometrium resulting from some abnormal overstimulation. This may in part be true, but as one sees hyperplasia of the endometrium frequently without hypertrophy of the wall, one must conclude that the hypertrophy develops secondarily as a work hypertrophy in an attempt on the part of the uterine wall to rid itself of the thickened mucosa. Muscle tissue and fibrous tissue occur in the same proportion as in the virgin uterus. The musculature in the gross appears coarser; this is due chiefly to hypertrophy of the individual cells. The muscle cells stain well and are increased in size rather than in number. In comparing the two fields, one in the hypertrophic uterus and one in the normal nulliparous uterus, the average shows that the fields in the hypertrophic uterus contain approximately three-fifths as many cells as similar fields in the nulliparous uterus. There is perhaps also some hyperplasia of the muscle cells, but this is difficult to determine. The coarser structure is evident microscopically and there is no evidence of infection or subinvolution.

#### CHRONIC METRITIS

Chronic metritis results from previous acute infection and is invariably seen as an extension of a chronic endometritis. A chronic endometritis is usually established secondarily to chronic salpingitis which in over two-thirds of the cases is primarily of



gonorrheal origin. Chronic metritis may also result from an acute process after abortion or in the puerperium, but not more than 10 to 15 per cent of the cases of chronic metritis are of this origin. A symmetrically enlarged uterus which may be associated clinically with pain, hemorrhage and leucorrhea; the pure chronic metritis type is present in not more than 15 per cent of such uteri removed at operation. The uterus is moderately enlarged. The cut surface is smooth in contradistinction to chronic subinvolution where the surface is uneven due to numerous thickened blood vessels appearing above the cut surface. Histologically there is a marked increase in connective tissue throughout the uterus, strikingly seen in the outer third of the wall, with a diffuse round cell infiltration throughout the thickness of the uterine wall and a tendency of the cells to group themselves around blood vessels and lymphatics.

Wilfred Shaw reinvestigated this subject in 1929. He feels that he cannot support the views of Goodall concerning the involution of the circulatory system of the uterus. He believes that the vessels of the uterus are reduced in size through atrophic changes in the walls which, in the case of the veins and sinuses, are peculiar in that a hyaline degeneration first occurs. The reduction of the lumen is mainly determined by proliferation of the subendothelial tissues. From our own observations in the past, we are more inclined to support the views of Goodall than those of Wilfred Shaw.

Shaw states that the elastic tissue content of the uterus is invariably increased after each puerperium, so that the uterus of a multipara who has borne many children always contains a large amount of elastic tissue. He regards this process as physiologic and does not consider that it determines the condition of chronic subinvolution.

It might be stated that the existence of degenerated tissue around the arteries of the inner third of the uterine wall varies in amount in different uteri. In some instances these complete or partial collars around the

artery are abundant and in other instances they are only seen inconspicuously. This would indicate, in my opinion, that they represent a residual condition and in no manner represent newly developed elastic tissue. The same can be said of the large plaques of tissue in the outer portion of the veins and in between the muscle bundles of the outer third. In a normal nulliparous uterus, the elastic tissue is found in fine strands. Newly developed elastic tissue in no way differs in character from this. I, therefore, consider the elastic staining substances as areas of degenerated tissue which have not been absorbed and, therefore, must be considered pathologic if present in any great degree, representing the picture characteristic of chronic subinvolution.

In a previous study, using the Fletcher Shaw classification in the examination of eighty uteri, I classified as subinvolution, thirty-eight; as chronic metritis, thirteen; as chronic subinvolution and chronic metritis combined, nine; hypertrophy, four; normal, eleven; and, senile, three.

I thought it might be of interest to go over a similar series to see how the present observations would classify these enlarged uteri. As a matter of fact, this classification was used routinely in specimens removed at operation. In a recent series, they were grouped similarly, but also included as a fourth lesion, the condition of diffuse adenomyosis. There were one hundred uteri and a diagnosis of chronic subinvolution alone was made in thirty-two cases; chronic metritis in eleven; hypertrophy in two; and, adenomyosis in four. The interesting feature of the study was the frequency of the overlapping of the above-mentioned conditions.

The combination of subinvolution with adenomyosis was found in eleven uteri; that of adenomyosis with hypertrophy in ten; chronic metritis with subinvolution in seven; chronic metritis with adenomyosis in four; and, chronic metritis and subinvolution combined with adenomyosis was found eight times. Other combinations also

existed, but to a lesser degree. We went over the sections separately and were especially impressed by the common association of early diffuse adenomyosis in these specimens.

Schwarz and McNalley previously called attention to the frequency of adenomyosis developing in the wall of uteri pathologically enlarged and considered the above mentioned pathologic conditions to have definite bearing on the development of so-called diffuse adenomyosis.

It is also interesting to note that in over 90 per cent of the cases where tubes were removed, chronic metritis was associated with chronic salpingitis, indicating that chronic metritis, per se, is comparatively uncommon.

Clinically the uterus reaches a fair state of involution, so far as size is concerned, by the eighth week postpartum. That is to say, it is almost the size of a normal multiparous uterus. The complete circulatory changes take somewhat longer and may take two or three months or longer until they are completed. I have always emphasized, in the prevention of subinvolution, that an examination be made between four and six weeks postpartum, preferably four, and that the position of the uterus be noted. If it is retroverted, irrespective of what its previous position was, for the individual, the uterus is brought forward and a properly fitting Smith pessary inserted. The patient is usually requested to return in a week or two and it is surprising to see what a

marked reduction in size is obtained in a period as short as a week. I feel that the postpartum uterus in a position of third degree retroversion favors a chronic pelvic congestion and as a result interferes definitely with involution of the circulatory system. The pessary should be worn at least six months, being removed at proper intervals for cleansing. Whether the uterus stays forward or not permanently, is not of so much importance. The more important thing is to keep the uterus in the proper forward position during the first six months postpartum, thus leading to more complete involution. I, therefore, feel that such a procedure, properly carried out, should lessen to a great extent the condition of chronic subinvolution. This condition by itself, in later years, can cause pain and hemorrhage and can lead to the development of other pathological lesions of the uterine wall. Hyperplasia of the endometrium itself, near the menopause as well as at other times, causes marked uterine bleeding. When associated with chronic subinvolution, this sign is often exaggerated.

#### REFERENCES

1. GOODALL, J. R. Studies from the Royal Victoria Hospital, Montreal, Vol. 2, No. 3 (Gyn. 11).
2. SCHWARZ, O. H. *Tr. A. A. Obst. & Gynec.*, 31: 316, 1918.
3. SCHWARZ, O. H., and McNALLEY, F. P. *Am. J. Obst. & Gynec.*, 6: 155, 1923.
4. SHAW, W. FLETCHER. *New System of Gynecology*. Eden and Lockyer, 2: 117. New York, Mac-Millan.
5. SHAW, WILFRED, J. *Obst. & Gynec., Brit. Emp.*, 36: 1, 1929.



## BOOK REVIEWS

MANUAL OF UROLOGY. By R. M. LeComte, M.D. Second Edition. Baltimore, 1939. Williams and Wilkins. Price \$4.00.

Since the first edition of this manual was published in 1935 so much progress in urology has taken place that the author found it necessary to rewrite practically the entire book. Sections on the neuromuscular physiology and pathology of the bladder and a chapter on impotence and sterility have been added. The author tells us, however, that inasmuch as these subjects are the basis of so much discussion and controversy they "may have to be changed soon, perhaps before this edition is out of the press"—refreshing frankness. This short book (295 pages) is an excellent introduction to the subject, which the student will do well to study before moving on to the larger textbooks and detailed monographs.

OFFICE GYNECOLOGY. By J. P. Greenhill, M.D. Chicago, 1939. Year Book Publishers. Price \$2.50.

Greenhill has written a compact, to the point, conservative, up-to-date volume, covering the office procedures in gynecology, and these alone. He has covered the field from the taking of the patient's history, to the gynecologic examination, gonorrhea in adults, the Rubin test, Elliott treatment, backache, vaginal douches, sterilization by coagulation of the uterine cornu, local anesthesia in the office, endocrinology, senile vaginitis, office urology, premarital examination and advice. The book is well written, 406 pages long, has a few necessary illustrations, and an index.

SURGERY OF THE EYE. By Meyer Wiener, M.D. and Bennett Y. Alvis, M.D. Philadelphia, 1939. Saunders.

The authors wrote this volume "to supply a handy atlas for the practicing ophthalmologist and student of ophthalmology [to which they] can quickly refer for information on the sur-

gical correction of ocular defects and disease." It is not a reference work containing every known method or suggestion, but only those procedures are offered which will *best* serve the purpose.

This work purposely leaves little to the descriptive text and imagination. An attempt has been made to illustrate in detail each operation selected. The artist, Dr. A. J. Hofsommer, sketched from actual scenes. The illustrations are numerous (396) and good.

CANCER OF THE COLON AND RECTUM. By Fred W. Rankin, M.D. and A. Stephens Graham, M.D. Springfield, Illinois, 1939. Charles C. Thomas. Price \$5.50.

Rankin and Graham have produced a comprehensive and up-to-date record of their experiences covering cancer of the lower gastrointestinal tract. The work of other surgeons in the field, both in this country and abroad, has been correlated and recorded. The book (358 pages, with nearly 150 illustrations) is a most complete presentation of the subject by recognized authorities.

THE RECTUM AND COLON. By E. Parker Hayden, M.D. Philadelphia, 1939. Lea & Febiger. Price \$5.50.

Dr. Hayden's book deals with the general subject of diseases of the rectum and colon, omitting unnecessary and nonessential details. The text is based largely on the author's personal experience, augmented by that of several co-workers at the Massachusetts General Hospital, where a clinic was organized to facilitate the diagnosis, treatment, and after-care of these disorders. For the most part the book deals with the surgery of the rectum and colon. The preparation of the patient, the details of the technique of the various operations and the after-treatment are fully described. The text is richly illustrated with photographs and drawings, especially prepared for this volume.

# The American Journal of Surgery

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A PRACTICAL JOURNAL BUILT ON MERIT

## EDITORIAL

### THE CONTRIBUTION OF DOG SURGERY TO THE SELF DEVELOPMENT OF THE PRACTICING SURGEON

**S**MALL town surgeons can easily provide themselves with facilities in their own community for practice in operating technique by utilizing dogs. A few years ago while we were engaged in postgraduate study we acquired enthusiasm for the surgical practice to be gained by operations performed on the dog. The money and time required to do this away from home, and the desirability of having opportunity for such experience from week to week, both for developing manual dexterity and for experimenting with new materials and techniques, led us to establish a set-up of our own for work of this sort. For the past eighteen months we have met one morning a week in the basement of an isolated home and have operated upon dogs for from four to six hours at a time.

Emphasis on preoperative diagnosis and preparation, surgical pathologic judgment, and postoperative care has given added meaning to the remark that "a surgeon is an internist who operates." But any man who operates knows that technical skill comes only with experience in performing operations. Such experience is never complete, for there are always new procedures to try, new ways of doing the old procedures, and new instruments and materials with which to work.

Recently, on a visit to some of the surgical centers of the east, we found that not only were the residents and younger surgeons availing themselves of dogs for surgical practice, but that more experienced men were also making active use of this type of training. To be sure, most of them had access to the dog surgery laboratories of undergraduate and postgraduate medical schools. They felt that it afforded a quite valuable adjunct to their own practice in surgery, and appeared to be interested that such a procedure was being used in a small community.

Dog surgery has been valuable to us because it has afforded opportunity for extensive experience in the use of instruments and suture materials, in the handling of living tissues, and in experimenting with unfamiliar operative procedures. It has given us what every surgeon covets—the opportunity to practice a wide variety of techniques, to develop ambidexterity, and to learn to think of technical problems which arise in the course of an operation in terms of tissues instead of personalities.

Some of the procedures which we have found practical in this work follow:

The abdominal wall of the dog resembles that in man, and leads itself quite well to experimentation with the various types of incisions described in the literature. The

anterior superior spine of the ilium is not so well defined as in man, but it is quite possible to demonstrate the structures pertaining to the two types of inguinal hernia and practice the repair of these tissues.

With the abdomen open in its upper portion the stomach is available for virtually every procedure which is carried out in the human patient. The cardia is somewhat less accessible in the dog due to the more conical shape of the diaphragm. This makes the procedure of total and subtotal gastric resection slightly more difficult. In the subtotal resection both the complete and partial stomas are employed. We find that these are among the most valuable operations that can be practiced on the dog.

The various types of gastrotomy and gastrostomy are performed, including the Spivack tubovalvular gastrostomy which provides, for a patient who has suffered obliteration of the esophagus, a mucous membrane lined tube through which feeding can be given without regurgitation of fluids through the tube. This operation can be performed on the dog, the cardia and pylorus tied off, and the stomach filled with a quart or more of water through a catheter in the gastrostomy tube. The catheter is withdrawn and the dog turned over. None of the water escapes from the stomach.

The various types of gastroenterostomy and pyloroplasty are also suitable for this work. There is no gastrocolic ligament in the dog; the dorsal mesogastrium forms a greater omentum but does not attach to the colon. However, in performing posterior gastroenterostomy a hole can be made in the mesocolon and the posterior stomach wall brought to this opening in the same manner as through a gastrocolic attachment were present.

The small bowel is ideal for practicing blind end closure, intestinal resection, and both open and closed methods of anastomosis, including lateral, end-to-end, and end-to-side. The wall of the bowel is slightly thicker and the lumen somewhat smaller than in man, and in some animals

more friable. This gives one the feeling that a procedure successfully carried out on these tissues is even more certain when done on the human patient. A young surgeon's first intestinal anastomosis is usually very clumsily done. Skill in this operation had much better be developed at the expense of the dog than at the expense of the patient.

The large bowel and the appendix are thick walled and for the most part distended with hard, dry feces, rendering them largely unsuitable for use. The appendix itself is usually about  $1\frac{1}{2}$  to 2 inches long and  $\frac{1}{2}$  to  $\frac{3}{4}$  inch in diameter.

The gall-bladder is suitable for nearly any procedure carried out on the human patient including cholecystotomy, cholecystostomy, cholecystectomy, and anastomosis to the stomach and duodenum. The common bile duct is rather small but its surgical treatment affords good practice.

The kidneys lie virtually within the peritoneal cavity and hence are not accessible by the extraperitoneal route. Indeed the peritoneum and the fascia transversalis are so thin that it is almost impossible to make an extraperitoneal approach to the ureters and other retroperitoneal structures. Through the abdomen, however, the ureters are readily available for end-to-end anastomosis and implantation into the bladder or bowel.

The uterus in the dog is a thin, Y-shaped, bicornuate structure and of no value to the gynecologist.

The thyroid gland, unfortunately, is very small and of little surgical value.

Thoracic surgery which has made such strides in the last ten years is usually possible in man without an artificial respirator. This is due to the fact that the human mediastinum is sufficiently rigid to permit, in most cases, opening the thorax and collapsing the lung on one side without serious respiratory embarrassment; only occasionally is it necessary to use positive pressure in the form of a tight mask and gas machine. In the dog, however, due to a thin, friable mediastinum, it is impossible

to expose the heart and one lung without collapsing both lungs. This problem has led us to develop a machine for positive pressure respiration for the dog, given by way of an intratracheal cannula. Lobectomy, pneumonectomy, and cardiac surgery have thus been added to the techniques available.

The respirator consists of a motor driven crank, stepped down until the crank makes 21 revolutions a minute and raises one arm of the bellows which handles about 2 liters of air at a time. No valves are employed. A garden hose is used, and at the point where the hose is connected with the cannula is a vent opening to the outside air. As the air is expressed from the bellows, part of it goes into the dog's lungs and part out of the bent. As the bellows open air is withdrawn from the lungs. This means, of course, that a portion of air is rebreathed. But another portion of fresh air comes in by the vent. This mixture is sufficient to preserve life satisfactorily. The open vent also prevents overdistention of the lungs by too much pressure.

Neurosurgery with cortical localization and various other procedures on the central nervous system may be practiced. There is unlimited opportunity for practice in the suturing of nerves and tendons, and the present day development of blood vessel surgery is in a large measure due to experience obtained on the dog.

An eye, ear, nose, and throat man who has interested himself in this work has found that the dog affords good practice work in esophagoscopy and bronchoscopy. The length of the dog's head is such that various instruments may not be long enough to work through the mouth and in such a case he approaches the bronchial tree by tracheotomy. This is occasionally necessary in man. The larynx may be used for laryngofissure.

The structures of the eye appear to be too thick and tough to be of much practical

value to the eye surgeon. The ear has not been used in our work.

We do not own a peritoneoscope set. However, we practiced with a direct vision cystoscope introduced through a 1 cm. incision into the dog's peritoneal cavity. With the familiarity thus obtained we have been able to use it with a better degree of understanding in selected human cases.

One of our urologic friends practices manual dexterity in the handling of the resectoscope by using the dog's esophagus.

We feel that our experience with the various types of suture material and needles has been worth while. We are indebted to Davis and Geck, Armour, Curity, Johnson and Johnson, and Scalan for their kindness in furnishing samples of catgut of all sizes, including 00000. Most of the work, however, is done with linen and silk thread of various sizes, always using the lightest thread and finest needles adaptable for the work in hand.

The development of facility in the handling of instruments, suture material, and tissues has been important to us. Also, in view of the fact that the young man in a small town operates infrequently, the major contribution to our experience has been practice gained in the more common surgical skills.

Only animals which are in the pound and which are to be exterminated anyway are used. The dog is handled and anesthetized in a manner which is much more humane than that employed in the dog pounds. There can be no sane criticism, providing the animal is in no way permitted to suffer pain. At the close of the operation the dog is killed by any of several humane means.

This form of training has been employed for many years in the teaching centers. We venture to suggest that it can make an even greater contribution to the self development of the practicing surgeon who does not have access to these centers.

CLYDE O. MERIDETH, JR., M.D.  
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# ORIGINAL ARTICLES

## THE CHANGING CONCEPTION OF CANCER OF THE PROSTATE

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NEW YORK CITY

FROM the very dawn of medical history, the prostate gland has been recognized as a source of misery to the male in the declining years of life. Notwithstanding the great progress that the ages have witnessed in the healing art, the prostate continues to hypertrophy as old age comes on. And side by side with benign hypertrophy, and indistinguishable from it in its early stages, there has stalked the specter of malignant disease of this organ, constituting one of the major problems among diseases of the genitourinary system. By the time symptoms of dysuria and retention have appeared, the cancer has as a rule metastasized, causing the prognosis to be, at best, a gloomy one. Not only was a fatal outcome to be looked for, but the patient's last days were made wretched with the discomfort of the inevitable suprapubic cystostomy in order to accomplish artificial drainage of the bladder.

The purpose of this paper is to call attention to a new attitude toward cancer of the prostate, which emphasizes the possibilities of immediate relief of symptoms without major surgery, as soon as there are signs of retention; and to point out, with a view to this end, the importance to every man 50 years of age or over of having a rectal examination of the prostate once a year as a matter of routine. The layman has little conception of the silent beginnings of malignancy that may be discoverable by the examining finger long before any urinary symptoms appear. Should the presence of a nodule, however small, be discovered, a biopsy specimen should

immediately be obtained to determine the nature of the induration.

Should symptoms already have arisen, modern surgery offers the sufferer the possibility of complete relief through transurethral prostatic resection, a procedure which enables him to live in comparative comfort and which also tends to prolong his life by relieving back pressure upon the upper urinary tract. He will be enabled to pass urine without discomfort, and, should the same symptoms of dysuria occur, a second, or a third resection can again be carried out, according to his needs, thus making it possible for him to live out the days remaining to him without the burden of wearing a permanent suprapubic drainage apparatus with all that this implies.

### INCIDENCE OF CARCINOMA OF THE PROSTATE

The frequency with which carcinoma of the prostate may be present in cases superficially appearing as benign hypertrophy was first mentioned by Albarran and Hallé<sup>1</sup> who, in the course of a study of one hundred specimens of prostatic hypertrophy in the Musée Guyon of the Necker Hospital, discovered malignancy in fourteen cases, or approximately 7 per cent. This led Young,<sup>2</sup> in 1905, to check up his own cases and to verify by exact figures the impression he already had that carcinoma of the prostate was more frequent than had been recognized. To his amazement, and that of urologists in general, he found in his clinical and pathologic material no less than 21 per cent of carcinoma among his cases of prostatic

obstruction. From Young we obtain also the following percentages as furnished by other writers: Oliver Smith, 16 per cent; Pauchet, 20 per cent; Davis, 20 per cent; Moullin, 25 per cent; Kuemmel, 20 per cent; Wilson and McGrath, 15.5 per cent; Freyer, 13.4 per cent; Institute of Pathology in Munich, 21 per cent.

Two recent reports, from Rich<sup>3</sup> and Moore,<sup>4</sup> working independently, confirm these figures. Rich of Johns Hopkins Hospital wrote, in 1935, that in 292 consecutive autopsies of male prostatics, forty-one proved to be cases of carcinoma (14 per cent). In two-thirds of these, the growth was too small to be recognized clinically. In eighty-two cases from the urologic service, seventeen (21 per cent) proved to be cancer. Moore, in the same year, after carrying out studies in two hospitals in Vienna, reported that he found in 375 prostatics sixty-three cases (16.7 per cent) of cancer of the prostate. Of these, fifty-two were occult and eleven manifest.

Myers<sup>5</sup> (1937) found a still larger percentage of carcinoma. Of seventy-five cases of prostatic obstruction examined in the Pueblo Clinic twenty-two proved to be malignant (29.4 per cent), while fifty-three (70.6 per cent) were benign hypertrophies.

Hoffman,<sup>6</sup> of the Prudential Insurance Company, discussing the figures of the United States Census Office with reference to the death rate per 100,000 male population from cancer of the prostate, states that deaths from this cause increased from 3.6 per cent in 1920 to 8 per cent in 1931, with a total of deaths from carcinoma of the prostate amounting to 38,486 in the twelve-year period.

Studies of the age groups in which cancer of this organ is liable to be found show the greatest number of cases in the sixth, seventh and eighth decades. Thus Moore<sup>4</sup> in his study of fifty-two occult cases, found none in patients under 40, but observed four cases in the fifth decade (41-50), six in the sixth, eighteen in the seventh, thir-

teen in the eighth, and seven in the ninth. In terms of percentage, Rich<sup>3</sup> observed in his 292 patients that 11 per cent showed cancer between the ages of 55 and 60, 21 per cent between 66 and 70, 28 per cent between 71 and 75, 37 per cent between 76 and 80, and 20 per cent between 81 and 90. Caulk and Boon-Itt<sup>7</sup> report that 93.9 per cent of their patients were over 50, and about 90 per cent were in the sixth, seventh and eighth decades. Bugbee<sup>8</sup> has operated on cancer of the prostate in patients from 45 to 97 years of age. Thompson and Emmett<sup>9</sup> found most cancers between 60 and 69, and the next between 70 and 79. The average age with Bumpus<sup>10</sup> was 65, and the average duration, in an untreated case, was thirty-one months.

Hager and Hoffman<sup>11</sup> (1937) reported that in their series of 396 cases, covering thirteen years, more than one-half had had symptoms for less than a year, and 50 per cent for less than six months.

Barringer<sup>12</sup> stated that in 98 per cent of his cases, when seen, the carcinoma had grown beyond the prostate. Graves and Militzer,<sup>13</sup> reviewing eighty-one cases of cancer with metastases, found that in all but six metastases to the bone were present. The total duration, where this was known, was from one to five years. Forty-three patients (53 per cent) survived less than nine months after demonstration of metastases.

Moore<sup>4</sup> found that metastasis and invasion outside the organ are a late manifestation, but that there is early invasion of the perineural lymphatics within the prostate. Dossot<sup>14</sup> emphasized the frequency with which the cancer invades the sacrolumbo-abdominal lymph nodes. Among thirty-six autopsies of cases of prostatic cancer he found that in thirty-four there had been invasion of the ilio pelvic lymph nodes, and in thirty-three, of the abdominal lymph nodes.

Bumpus<sup>10</sup> demonstrated metastases in 243 of 1000 cases at the Mayo Clinic. Where these were present, he too had an average survival of nine months. There



were only twenty-one five-year cures among 164 patients submitted to prostatectomy (forty-seven perineal, 117 suprapubic).

#### EARLY RECOGNITION IMPORTANT

We see, therefore, that carcinoma of the prostate is a widespread condition, and that unless it is clinically recognized before it has metastasized the patient is already beyond any but palliative treatment. If, on the other hand, the first small signs of a nodule are discovered and recognized by digital examination of the rectum, there is still room for hope that perineal prostatectomy may accomplish arrest of the process. If the disease is not already too extensive, a radical cure can be obtained. Young<sup>2</sup> states that his statistics show cures in over 50 per cent of cases in which the prognosis was at all favorable. G. G. Smith<sup>15</sup> after radical operation on fifty early cases, reported that seventeen (33 per cent) were alive and well one to eight years after operation. A substantial number of five-year cures of early cases have also been reported by Marion,<sup>16</sup> Yllyes,<sup>17</sup> Wildbolz,<sup>18</sup> and others. According to Caulk,<sup>19</sup> however, prostatectomy is applicable in only 3 to 5 per cent of any surgeon's cases, and he would hesitate to propose it because of the difficulties of being sure that the disease was confined to the gland. "The majority of operators," says Caulk, "have as their hope, of course, to cure the disease, but actually they strive at the postponement of death and alleviation of the symptoms."

For this reason, it cannot be too strongly emphasized that men over 50 should be warned of the possibility of a silent carcinoma of the prostate, and instructed as to the importance of routine examinations once a year to discover the actual conditions of this organ, so that, if the least sign of a carcinoma exists, the beginning growth in the prostate may be removed while it is still operable. If such an examination should reveal the presence of

cancer, the earlier this is known the better will be the prognosis. The great majority of patients today wait until urinary symptoms appear and until they are beyond the stage in which a radical procedure can be carried out. For such individuals, however, it is unquestionable that transurethral resection, when properly done, prolongs life and gives great relief without extensive surgery.<sup>20</sup>

In cases so far advanced that toxemia and uremia have already resulted from obstruction, it is startling to see how much may even yet be accomplished by this modern means of securing drainage. Many of these cases respond almost miraculously and can be restored to a fair degree of health and usefulness even though the cancer has metastasized. Although these patients will ultimately die of cancer, they escape the torment of intolerable urinary symptoms and have the prospect of succumbing to a metastasis with far less pain than that which attends the late stages of cancer of the prostate.

After removal of the carcinomatous obstruction by transurethral resection, it is still possible to control pain and prolong life by use of x-rays or radium treatment. Indeed, as a means of relieving pain the value of these radiologic methods in selected cases and in suitable dosage is beyond question when cure is no longer a possibility.

This modern transurethral procedure, or closed method of approach, when carried out in competent hands, not only relieves symptoms but also avoids the common complications that are encountered when the open method of surgery is used for advanced cases. In fact, bothersome perineal fistulas, both urinary and fecal, as well as urinary incontinence, are entirely eliminated by the transurethral method. In addition this procedure obviates the long suffering and annoyance following a suprapubic cystostomy, with its burdensome sequel of a catheter life.

In my own clinical experience with carcinoma of the prostate I have observed

that patients operated upon by this conservative method live longer, have less urinary distress, less reaction and inconvenience, and, on the whole, are much more comfortable, besides being saved the disadvantages of a long stay in the hospital for radical treatment of a condition which is already hopeless.

#### CLINICAL CONSIDERATIONS

With regard to operability, three clinical types of cases may be recognized. We may group these as follows:

Group I. Silent or occult cases (operable).

Group II. Circumscribed cases, with the malignant growth still confined within the capsule (still operable).

Group III. Diffuse cases of carcinosis (inoperable).

The existence of a cancer in any of these groups can be discovered in most cases by rectal examination. Digital palpation within the rectum will discover the form, shape and consistency of the prostate, and will reveal any nodulation or irregularity of the surface of the gland. In the hands of one who has been properly trained for it, this examination will, in most instances, suffice for a diagnosis of carcinoma of the prostate. Cancers even as small as half the size of a pea have been revealed by this procedure. To one who is accustomed to this type of examination, the finding of such a nodule is easily recognizable as suggestive of cancer. The diagnosis can be verified by needle biopsy, which in about 70 per cent of cases will yield a positive finding.

But it is obvious that if a carcinoma is to be discovered in time for a cure, it will be brought to light ordinarily only in the course of a general physical examination, for at the outset there are no urinary symptoms to bring the patient to a urologist. Such an examination will, therefore, in the nature of things be conducted by a general practitioner. Too often this general physical examination does not include, as it should in all men over 50, an examination of the prostate gland. It is of great impor-

tance, accordingly, that every student in every medical school be taught to make this examination and to interpret its results. In the future we may expect that no student will be allowed to engage in medical practice who has not acquired proficiency in the technique of rectal palpation of the prostate, and the interpretation of the findings.

*Group I. Silent or Occult Cases.* In this group the patient has no symptoms of any kind relating to the prostate or the urinary system, nor is there anything in the history to suggest metastases. He is being examined solely as a routine procedure, as a precautionary measure for his own protection against possible future trouble. It is unfortunate that the individuals composing this group do not, as a rule, develop urinary symptoms until late. Urinary manifestations which might attract attention to the existence of a carcinoma are usually much slower to appear than in a case of benign prostatic hypertrophy.

It is estimated that about 10 per cent of cases can be diagnosed rectally early enough to permit cure of the cancer by a radical perineal prostatectomy. Since the posterior lobe of the prostate is the site of predilection for carcinoma, being the primary seat in about 80 per cent of cases, whereas benign hypertrophy begins more frequently in the median or lateral lobes, we have at once a clue to the probable significance of any marked induration in the posterior lobe that may be felt by the examining finger, especially if such hardness is in the form of a nodule or an irregular surface of stony-hard consistency. (Fig. 1A.) Palpation of such a nodule upon a sound or on the cystoscope renders its differentiation from a calculus easier. If such a nodule is felt, and there is any room for doubt, needle biopsy may clear up the diagnosis.

In any event, upon discovery of a nodule, urethrocystograms should immediately be taken, as well as plain roentgenograms to reveal whether stone, local

# CANCER OF PROSTATE

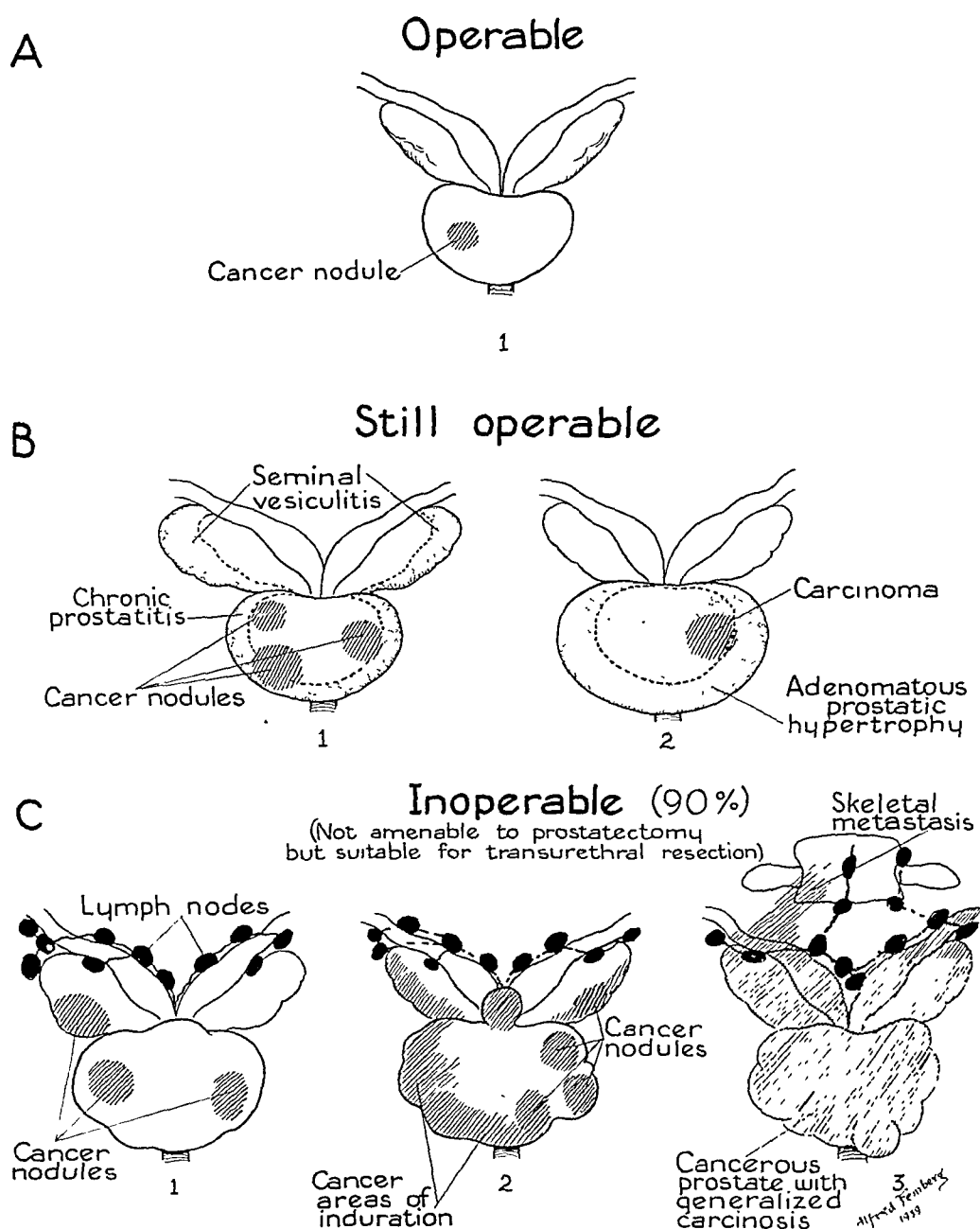


FIG. 1. Schematic representation of the three clinical groups of cancer of the prostate most commonly observed, from the point of view of operability and cure. A, silent or occult group without symptoms, in which the minute cancer nodule can be detected by rectal palpation and in which total prostatectomy will accomplish cure. B, circumscribed group, in which the cancerous lesions have not extended beyond the capsule but in which urinary symptoms have appeared. 1, the fibrous type of prostate with evidence of chronic prostatitis and seminal vesiculitis in which the presence of stony hard nodules reveals the concomitant cancerous lesion. 2, the adenomatous type of prostatic hypertrophy associated with carcinoma. In both of these types the malignant lesion is circumscribed and is still amenable to prostatectomy. C, the diffuse group, in which generalized carcinosis has arrived, with a fixed gland and clinical evidence of metastasis, indicating that the malignant growth has spread beyond the capsule and is already inoperable. 1, the growth has invaded the seminal vesicles and lymph nodes of the prostatovesicular space. 2, the cancerous area of induration within the gland has expanded, with multiple nodular infiltrations and invasion of the periprostatic structures. 3, the late stage of generalized carcinosis is shown, with multiple skeletal metastases, advanced encroachment upon the prostatomembranous urethra, and invasion of the bladder neck and surrounding structures. Cases in Group C, which unfortunately comprises 90 per cent of cases seen by the urologist, can be relieved of their urinary sufferings, and their life span materially prolonged by the modern method of transurethral resection. (See text, Clinical Considerations.)

extensions, or bony metastases are present. The urethrocytogram will reveal whether any changes have occurred in the outline of the prostatic urethra, the vesical orifice or bladder. Routine x-ray studies will show whether there are metastases in the bony pelvis, the sacrum, the ilium, the lumbar vertebrae or chest, these being as a rule the first skeletal structures to be invaded. They will also differentiate a possible calculus. One should remember, however, that it is possible for a calculus and a cancerous nodule both to be present. If stone can be excluded, the hard, irregular, nodular prostate is easily recognizable as carcinomatous. In this case, further digital examination of the rectum will reveal whether the growth has invaded the seminal vesicles, which are in 50 per cent of cases the next tissue to be involved. If these are found to be of normal consistency, and the x-ray examinations are negative for metastases, it can be safely assumed that the growth is still confined within the capsule of the prostate itself. It is, therefore, amenable to early removal by means of a radical prostatectomy.

In the autopsy findings of Mintz and Smith<sup>21</sup> upon 100 cases of cancer of the prostate, only thirteen cases could be regarded as of this early type. These thirteen patients had died of unrelated diseases, while the malignant growths still remained occult and without evidence of metastases.

*Group II. Circumscribed Cases.* In this group, urinary symptoms have appeared, for which the patient seeks relief at the hands of a physician. There is frequency of urination day and night and some dysuria, and anything from a slight amount of residual urine to complete retention. But examination reveals that the prostate is elastic in consistency and is still freely movable from side to side, showing that the lesion is still circumscribed to the gland and has not extended beyond the limits of the capsule. There may, however, be one, two or three stony hard nodules involving the posterior lobe, or the right or left

lateral lobes, but no evidence to the palpating finger of involvement of the seminal vesicles, ampullae or intervesicular space, and no adhesions to the rectal wall, although there may be evidence of chronic prostatitis and seminal vesiculitis. (Fig. 1B—1.) In some of these cases the cancer grows very slowly, especially where fibrous tissue predominates. Denonvilliers' fascia for a long time proves an adequate protection against extension toward the rectum.

A prostate gland removed with a diagnosis of simple hypertrophy frequently contains nodules of malignant degeneration (about 13 per cent). In cases where carcinoma and benign adenomatous hypertrophy exist at the same time within a prostate, the patient is likely to visit his physician earlier, since as a rule the benign hypertrophy causes urinary distress and frequency earlier than does the cancerous nodule, which is usually in the posterior lobe where it does not encroach upon the urethra and bladder neck. Many of these cases, therefore, may be discovered at an earlier stage than those of group 1, which is a factor greatly in their favor, from the point of view of prognosis. (Fig. 1B—2.) Pasteau<sup>22</sup> holds that the surgeon who makes it a practice to remove a prostate gland for simple hypertrophy is, in effect, controlling cancer of the prostate gland. When such a carcinoma comes under observation, while the prostate is *still movable*, and the adjacent structures have not been invaded, that is to say, while it is still confined within the capsule, it is amenable to removal by a total radical prostatectomy. Cases in which this procedure has been carried out at this stage have been reported by various authors; there has been no recurrence, and the patients could be pronounced cured, having lived for many years afterward in excellent health. Hence, if we can get hold of these cases while the malignant growth is still limited within the capsule, and while the gland is still freely movable beneath the finger, with no adhesions to the surrounding tissues, we can with

every confidence look forward to complete cure, by an operation no more perilous than that which is done every day for benign prostatic hypertrophy. In all cases where the prostate can be enucleated entire, there is no reason to hesitate to do the total operation. Carefully selected cases in groups I and II successfully cured by radical prostatectomy, surviving for long years afterward without recurrence and free from urinary troubles of any kind, have been reported by Young,<sup>2</sup> Freyer,<sup>23</sup> Hinman,<sup>24</sup> Marion,<sup>16</sup> Wildbolz,<sup>18</sup> Yllyes,<sup>17</sup> Rolnick,<sup>25</sup> G. G. Smith<sup>15</sup> and others.

Total perineal prostatectomy involves removal of not only the prostate, but also of the seminal vesicles and ampullae, the bladder neck, and most of the fascia about the prostate. All the structures between the ureteral orifices and the membranous urethra are resected, after which the bladder neck is united to the membranous urethra. The external sphincter is not disturbed, and the patient preserves his continence.

Radical suprapubic prostatectomy implies the removal of the prostate and its capsule with the bladder neck, the seminal vesicles and their ampullae all in one piece through the bladder as described by Marion<sup>16</sup> and also by Pauchet.<sup>26</sup>

In carefully selected cases one or the other of these radical operations should be chosen, when the surgeon is convinced that the malignant growth is still circumscribed to the prostate. In this group simple enucleation is not enough, for in most cases it causes spread of the cancer, many instances having been observed in which the carcinoma has invaded the remaining capsule and has extended into the bladder neck and trigone. Some of these prostatic carcinomas are of extreme malignancy, and metastasize very early. The safest course, therefore, if the growth has not yet penetrated the capsule, is to perform the radical perineal operation, in which the immediate operative mortality is less and the patients appear to live longer than when the suprapubic operation is done.

When this is carried out under proper indications and by the improved methods of the most modern technique, the results are very encouraging.<sup>20</sup>

Nevertheless, in *borderline* cases, in which there is evidence of adenomatous hypertrophy with an induration or a nodule somewhat suggestive of carcinoma but no evidence of metastasis or extension, most urologists are in accord that a simple early enucleation is sufficient and that this is the best operative choice under the circumstances. In the event then that the histologic examination of the specimen removed at operation reveals malignancy, the patients of groups I and II should receive, as a prophylactic measure, a routine postoperative course of deep x-ray treatments, preferably repeated every six months, and designed, if not to effect a cure or to check the spread of the disease, at least to control and mitigate the painful symptoms which will ultimately develop. Some urologists instead use implantation of radon seeds or a combination of these with x-rays. The use of x-rays without radon seeds, however, seems to be less irritating and more soothing as a means of relieving pain and urinary distress.

*Group III. Diffuse Cases. Carcinosis.* In 90 per cent of the cases that are seen, the carcinoma has already spread beyond the capsule and cannot be removed. The gland, of stony hardness, has become fixed and immovable. Rectal examination now reveals in addition an increased resistance in the intervesicular space just above the prostate. This results in an elevation of the subtrigonal plateau, easily recognized in the cystoscopic examination. The interlobular sulcus in the prostate itself is found obliterated, and the circumference of the gland is irregular and somewhat nodular. The seminal vesicles are distended and sometimes full of nodular infiltrations, revealing the extension of the disease.

Urinary disturbances have become very troublesome in most of these advanced cases as the result of obstruction to the outflow of the urine, although in many the

gland may be actually small or atrophic. In Caulk's series 35 per cent were of this type; but they were much more virulent and metastasized much more quickly than those of large size. Notwithstanding the smallness of the primary growth in such cases, metastases are present at a very early stage in the disseminating type. (Fig. 1C, 1, 2, 3.) In many of these cases the patient is suffering from arthritis, sciatic pain or lumbago, and a plain roentgenogram discloses that these symptoms are due to multiple bony metastases. In other cases, of scirrhous type, the cancer may give rise to little or no inconvenience of any kind. The patient is unaware of his danger, and the case does not reach the surgeon until all hope of eradication of the growth is past.

In no other type of carcinoma is it so tragically true as in that of the prostate that by the time it is diagnosed clinically it is already too late to operate or to give any but symptomatic treatment. In all these cases generalized metastasis has taken place into the lymphatics and their lymph nodes, involving the skeletal system, the bronchopulmonary and mediastinal regions and other internal organs. There is direct extension into the bladder, ureters, and, more rarely, into the membranous urethra, the corpora cavernosa, glans penis, perineum and rectum. But as a rule the seminal vesicles and the lymphatics of the prostate and the inter-vesicular space are the first tissues to be invaded. Not only frequency and painful urination, with marked nocturnal dysuria, but also hematuria, bladder tenesmus, incontinence and complete retention with pain in the rectum and perineum are among the cardinal symptoms observed in these late cases. In addition the back pressure due to the retention results in ascending infection, with marked dilatation of the ureters and pyelonephritis, leading finally to pyoureters, pyonephrosis and a terminal picture of uremia and cardiorenal failure.

#### TRANSURETHRAL RESECTION

When a cancer has reached this third stage and has cleared the capsule, only palliative treatment is applicable. But no longer are we compelled to have recourse to suprapubic drainage and the wearing of a permanent catheter, which until recently constituted the only "palliative" available for symptoms of urinary obstruction, after these had become established. When Young in 1909 announced his "punch" operation for endoscopic removal of bladder neck obstructions, followed in 1910 by Edwin Beer's successful application of the high frequency current to tumors of the bladder by way of the cystoscope, the full significance of these innovations in urosurgical technique was little realized. It took years for the technique to be perfected and years for the requisite experience in its handling to be acquired, before its full value and its relative safety could be recognized. Today, in the hands of an expert, the mortality rate from this procedure is less than 2 per cent.

Only within the last seven years has the use of this method become sufficiently general for its applicability in cases of hopeless, incurable cancer of the prostate to be appreciated. It has enabled these patients to be relieved completely of their urinary sufferings and to live a normal life for at least months, and not infrequently for years, while the carcinoma has pursued its inexorable march. The procedure has overcome back pressure upon the upper urinary tract, and caused the menace of residual urine to be abolished. Some who have come even in a state of pronounced toxemia have been restored to improved vitality and have lived a life of relative comfort for varying periods. Of 129 cancer patients upon whom Caulk<sup>19</sup> operated with the cautery punch, 30 per cent were living after three years, 18 per cent after four years, 12 per cent after five years, and 5 per cent after seven or more years.

It has been objected by some surgeons, especially of the French school, that by deliberately cutting through the tissues

of a malignant growth one of the most elementary principles of surgery is violated. A cancer should either be removed in toto, or not touched with the knife at all. Thus we find Chevassu<sup>27</sup> saying that a transurethral resection is like the lash of a whip to the growth of a prostatic cancer. Experience, however, does not show this to be the case. All urologists who have used this method extensively will be inclined to agree with Jacobs'<sup>28</sup> statement that with a patient in whom the prognosis is inevitably going to be downhill, this consideration need be no deterrent to a procedure which aims at relieving the urinary obstruction and not at a curative effect. When it has become evident that the cure of a sufferer is out of the question, the first concern of the surgeon should be to relieve pain rather than to prolong, for a brief span, a life that has become, at best, a burden without such relief.

In carrying out a transurethral resection, it has been found that carcinomatous tissue is trimmed away with more ease than benign hypertrophied tissue and that as a rule there is less hemorrhage. Few bleeding points have to be coagulated during operation. Carcinoma of peripheral type with growth at the neck of the bladder lends itself better to resection than that which has invaded the prostatic urethra, where resection may be technically more difficult. This procedure is especially indicated in cancers of slow growth. The presence of metastases is not to be regarded as a contraindication. No good reason can be adduced for failure to relieve urinary symptoms that are causing distress, while the carcinoma is progressing in some other part of the organism.

Transurethral resection may thus be regarded as a means of enabling the patient to utilize to the best advantage the time left to him by the cancer, which may be shorter or longer, but which apparently is not affected adversely in its duration by this beneficent palliative operation. He will be able to escape the bondage entailed by a suprapubic fistula and a permanent

catheter life, and to live with his family in comparative comfort, a burden neither to himself nor to others. And in not a few such cases, death has been the result of an intercurrent disease, and not of carcinoma. Again, in cases where there has been extensive metastasis, death often comes as the result of this process instead of from the primary carcinoma, with its many agonizing features. It may come from metastatic processes, the pain of which it is much easier to control, by suitable measures, than the intolerable suffering of the man dying from cancer of the prostate, with its imperious urgency and dysuria. In cases where the prostatopelvic carcinosis is so extensive that it is producing great distress and is causing intolerable radiating or localized pain, it is possible to bring symptomatic relief of these manifestations by the routine use of deep x-ray treatment. In addition to this method of radiation for the relief of pain, some authors advocate the implantation of radon seeds or radium needles with a view to controlling the disease by reducing the size of the gland; but this type of radiation as a rule has not only been painful, but has also caused many complications, and the results up to the present time have on the whole been disappointing.

Although no one method of treatment has been entirely satisfactory in this group, it appears that the best choice of treatment in our present state of knowledge is transurethral resection to relieve obstruction, followed by courses of deep x-ray treatments, to control the dissemination of the disease and to minimize the painful symptoms arising from the original lesion and its metastases.

It is not to be denied, however, that there are advanced cases, in which the prostate has become so fixed and the caliber of the urethra so narrow that neither a sound nor the small resectoscope can be passed. In such cases a permanent cystostomy is, of course, still in order as the best means of relieving back pressure and urinary distress. But when the cancer-

ous lesion has extended up into the bladder and ureters, even cystostomy may fail to give relief and the only possible recourse is to divert the urine by bilateral transplantation of the ureters. It may be said, however, that in well chosen early cases of groups I and II when the biopsy reveals that the gradation of the malignancy is still of type I or 2, or histologic examination of the specimen removed by transurethral resection shows an early type of malignancy, the radical perineal prostatectomy should be offered to the patient as the best opportunity to attain permanent cure. But when the biopsy reveals that the malignant lesion is already of type 3 or 4, it is too late to contemplate a permanent cure by a total prostatectomy. Also in those late cases of group III that histologically belong to type 3 and 4, when the malignancy has already metastasized and the prognosis is hopeless, the procedure of choice should be the palliative method of transurethral resection for relief of the obstruction and the urinary distress.

It is important that all fragments of tissue removed for the purpose of biopsy be properly examined. Material removed by transurethral resection should all be saved, since in a large number of cases the diagnosis can be verified by its examination. For this purpose I<sup>20</sup> have devised a "fishing net" to be attached to the resectoscope to facilitate the collection of all prostatic material resected, since this will frequently be the key to the diagnosis.

#### SUMMARY

The toll of cancer of the prostate in men over 50 years of age is so great as to constitute one of the major problems in urology. Until quite recently urologists have adopted a defeatist attitude, and have assumed that cases no longer amenable to prostatectomy (which meant the great majority) must face the inevitability of a suprapubic cystostomy, with all the sufferings entailed by a catheter life, in order to relieve urinary symptoms. The

life thus prolonged for a few months or years had little attraction for its victims or their households.

Within recent years, however, a new attitude has arisen toward malignant diseases of the prostate, which emphasizes the possibility of immediate relief of urinary symptoms in hopeless cases, without the use of major surgical procedures. In such cases, as soon as the encroachment of the malignant growth upon the bladder neck and urethra begins to cause symptoms of dysuria and retention, the urologist may now relieve these symptoms by transurethral resection of the offending portion of the prostate, a procedure of great simplicity in the hands of one experienced in its execution. Should the same symptoms develop again later on, the same procedure is again available, as often as seems necessary.

However, with the means of early diagnosis that are now available, there is no necessity for the great number of deaths from cancer of the prostate that have been observed up to the present time. These have been due largely to the silent manner in which these carcinomas usually develop. The early beginnings can now be discovered and recognized by any physician who has been trained to make routine examinations of the prostate by way of the rectum. Long before any urinary or other symptoms appear, the examining finger may discover the presence of a stony hard nodule in the posterior lobe of the prostate, in men over 50 years of age.

Men who have reached this critical age should, accordingly, as a prophylactic measure have routine examinations of the prostate once a year, so that if the least sign of such a nodule is discovered, the growth may be totally removed before it becomes inoperable. Since these patients have no urinary symptoms to bring them to the urologist, it is important that every general practitioner learn the technique of such an examination, and emphasize its importance to all elderly men who come for a general physical examination.



When such a nodule is found, a needle biopsy should immediately be done to confirm or refute the suspicion of carcinoma. If the biopsy findings are positive, and the x-rays show no metastasis, perineal prostatectomy at this early stage will in most cases accomplish complete cure.

Cancer of the prostate may, according to its stage and treatment, be divided into three groups:

Group I consists of silent or occult cases, with no symptoms. These are amenable to prostatectomy.

Group II consists of cases which are circumscribed, still confined within the capsule of the prostate, but in which urinary symptoms have appeared. So long as the gland is freely movable, it is evident that the adjacent structures have not been invaded, and the growth is still amenable to a total radical prostatectomy.

Group III consists of cases in which the carcinoma has spread beyond the capsule, and cannot be removed. Of the cases seen, 90 per cent fall within this group at the present time. Metastasis has occurred into the lymphatic and osseous systems, and besides urinary symptoms the patient is usually suffering with arthritis, sciatic pains, lumbago, or other type of pain due to perineural invasion or invasion of the skeletal system. In addition to local symptoms and the presence of a general induration of the entire region surrounding the prostate, the patient is affected with a generalized carcinosis. Prostatectomy is no longer available. These cases lend themselves, however, to transurethral resection for relief of urinary distress.

The purpose of this paper is, first, by urging early examination, to bring into group I and II many of the cases that would otherwise reach the condition of group III, cases that reach the surgeon too late for eradication of the growth; and secondly, to emphasize the ease with which those who are so unfortunate as to have reached the status of group III, may still have their urinary symptoms relieved or even wholly abated, and their lives mate-

rially prolonged in comfort, by undergoing transurethral prostatic resection.

The objection traditionally raised against incision of a malignant growth, that it may give rise to metastases, has no weight here, since there is admittedly no hope of cure in these group III cases. The patient is already full of metastases, so that their avoidance is no longer a consideration. The main object of the surgeon should now be to relieve symptoms as they arise, and especially to obviate the sufferings of a catheter life such as these patients have in the past been compelled to lead. The use of x-rays for relief of pain and to control metastasis is also recommended.

About 5 per cent of group III will not be amenable to transurethral treatment, owing to the impossibility of passing any kind of instrument into the urethral canal upon which the carcinoma has encroached. For these patients, suprapubic drainage, or, as an alternative, possible transplantation of the ureters, must still remain the only means of relief.

#### CONCLUSIONS

1. Carcinoma of the prostate is more common than is suspected; in fact, it is three times as frequent as cancer in any other internal organ of the male.

2. Carcinoma of the prostate is now known to be present in about 20 per cent of all cases of prostatic obstruction.

3. All men over 50 years of age should be subjected to routine rectal examinations, with a view both to discovering the possible existence of a cancer nodule in the prostate, and to preventing its further development.

4. Three groups of cases are presented from the point of view of operability and cure.

5. In early cases cure can be obtained by total perineal prostatectomy.

6. Advanced cases with evidence of metastasis, which unfortunately constitute about 90 per cent of all cases at the present time, are not amenable to radical operation or cure.

7. These inoperable cases can now, however, be relieved of their painful symptoms and urinary obstruction by the modern procedure of transurethral resection.

8. Transurethral resection should be carried out only by a competent urologist, experienced in this new method of treatment.

9. Transurethral resection should never be considered for an early case, which is amenable to cure by radical operation.

10. After operation, the patient should receive deep x-ray treatments to control metastases and to relieve pain and urinary distress.

11. More cases of carcinoma of the prostate could have been cured if the diagnosis had been made "early" enough to let the specialist-surgeon carry out a conservative radical perineal prostatectomy.

12. The prognosis for a five-year cure is greatly improved under this new conception of the management of carcinoma of the prostate.

#### REFERENCES

- ALBARRAN and HALLÉ. Hypertrophie et néoplasies épithéliales de la prostate. *Ann. d. mal. d. org. gén. urin.*, p. 113, 1900.
- ALBARRAN, J. Tumeurs malignes de la prostate. In: *Traité de chirurgie clinique et opératoire*, 9: 680-714, Paris, 1900. Le Dentu et Delbet.
- ALBARRAN, J. Médecine opératoire des voies urinaires. Prostate. Paris, 1909. Masson.
- YOUNG, H. H. The radical cure of cancer of the prostate. *Surg., Gynec. & Obst.*, 64: 472-484, 1937.
- YOUNG, H. H. Cancer of the Prostate. In: *Cabot's Modern Urology*, Chapt. 19. Philadelphia, 1936. Lea & Febiger.
- YOUNG, H. H. The ultimate results in the treatment of carcinoma of the prostate by the radical removal of the prostate, vesical neck and seminal vesicles. *J. Urol.*, 29: 531-543, 1933.
- RICH, A. R. On the frequency of occurrence of occult carcinoma of the prostate. *J. Urol.*, 33: 215-223, 1935.
- MOORE, R. A. The morphology of small prostatic carcinoma. *J. Urol.*, 33: 224-234, 1935.
- MYERS, G. M. The occurrence of carcinoma in clinically benign prostatic obstructions. *Colorado Med.*, 34: 248-251, 1937.
- HOFFMAN, F. L. Cancer of the prostate and prostatic diseases. *New England J. Med.*, 210: 507-512, 1934.
- CAULK, J. R., and BOON-ITT. Carcinoma of prostate. *Am. J. Cancer*, 16: 1024-1052, 1932.
- BUGBEE, H. G. Cancer of the prostate. *Tr. A. A. Genitourin. Surgeons*, 29: 207-212, 1936.
- THOMPSON, G. J., and EMMETT, J. L. Treatment of carcinoma of the prostate gland by transurethral methods. *Urol. & Cutan. Rev.*, 39: 679-685, 1935.
- BUMPUS, H. C. Carcinoma of the prostate. A clinical study of 1000 cases. *Surg., Gynec. & Obst.*, 43: 150, 1926.
- HAGER, B. H., and HOFFMAN, E. F. Statistical data on 395 cases of carcinoma of the prostate. *J. Urol.*, 37: 180-185, 1937.
- BARRINGER, B. S. Phases of the pathology, diagnosis and treatment of carcinoma of the prostate. *J. Urol.*, 20: 407-411, 1928.
- GRAVES, R. C., and MILITZER, R. E. Carcinoma of prostate with metastases. *J. Urol.*, 33: 235-251, 1935.
- DOSSOT, R. Les origines et les extensions du cancer de la prostate. *Arch. urol. de la clin. de Necker*, 5: 257-311, 1927.
- SMITH, G. G. Total perineal prostatectomy for carcinoma. *J. Urol.*, 35: 610-617, 1936.
- MARION, G. À propos du traitement du cancer de la prostate. *J. d'uro.*, 21: 385-396, 1926.
- YLLYES, G. v. Erfahrungsergebnisse bei Nieren-, Blasen- und Prostatakrebs. *Ztschr. f. urol. Chir.*, 41: 123-132, 1935.
- WILDBOLZ, H. Die Erfolge operativer Therapie des Prostatacarcinoms. *Schweiz. med. Wchnschr.*, 29: 726, 1928.
- CAULK, J. R. Carcinoma of the prostate. *J. Urol.*, 37: 832-839, 1937.
- GUTIERREZ, R. Transurethral treatment of bladder neck obstructions: Endoscopic prostatic resection. In: *History of Urology*, chapt. 5, 2: 137-186. Baltimore, 1933. Williams and Wilkins.
- GUTIERREZ, R. Later results of surgery of the seminal vesicles. Report of one hundred consecutive seminal vesiculectomies. *J. A. M. A.*, 93: 1944-1951, 1929.
- GUTIERREZ, R. Surgery of the seminal vesicles, ampullae and vasa deferentia. In: *Oxford Loose-Leaf-Surgery*. Chapt. 9, 3: 300-509. New York, 1935. Oxford University Press.
- GUTIERREZ, R. Primary carcinoma of Cowper's gland. *Surg. Gynec. & Obst.*, 65: 238-248, 1937.
- GUTIERREZ, R. A new device for catching tissue in endoscopic prostatic resections. *Urol. & Cutan. Rev.*, 38: 91-93, 1934.
- MINTZ, E. R. and SMITH, G. G. Autopsy findings in 100 cases of prostatic cancer. *New England J. Med.*, 211: 479-487, 1934.
- PASTEAU, O. Quoted in A Review of Urologic Surgery. *Arch. Surg.*, 37: 840, 1938.
- FREYER, P. J. Cancer of the prostate. *Urol. & Cutan. Rev.*, 18: 69-75, 1914.
- HINMAN, F. The Principles and Practice of Urology. Philadelphia, 1935. W. B. Saunders.
- ROLNICK, H. C. Radical perineal prostatectomy for carcinoma. *J. Urol.*, 34: 116-121, 1935.
- PAUCHET, V. Le traitement du cancer de la prostate. *Paris chir.*, 16: 4, 1924.
- PAUCHET, V. Tumeurs malignes de la prostate. *Encycl. fr. d'Urol.* 6: 281-360, 1923.
- CHEVASSU, M. Quoted in A Review of Urologic Surgery. *Arch. Surg.*, 37: 843, 1938.
- JACOBS, A. Transurethral resection of the malignant prostate. *Brit. J. Urol.*, 7: 321-329, 1935.

# CYSTOTOMY FOR STONE IN CHILDREN

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IN Hippocrates' time, lithotomy was performed by specialists. Perhaps this is the most ancient major surgical procedure which is still in use. Great progress in medical sciences has been made, but we are still using this operation, and we are still relatively ignorant of the real nature of the malady.

Urinary stones are manifestations of a variety of diseases. But there is reason to believe that nearly all of the cases of bladder stones during the first few years of life belong to one etiologic group. Many cases have been reported from the countries of southern Asia.<sup>3,4,6</sup> A few cases have been reported in the United States.<sup>1,2,5</sup> There is said to have been a marked decrease in the incidence of the disease in England, Germany and France during the past few generations.<sup>3</sup>

The disease is not rare in Syria. In four years at the American Presbyterian Hospital in Tripoli, Syria, sixteen children with urinary calculi came under treatment: thirteen bladder stones, two urethral stones, and one ureteral stone. Also, the author collected 125 such stones from six other surgeons in Syria and Palestine.\* The results of a study of some of these specimens and considerations of etiology will be published elsewhere. Suffice it to say here that the geographic distribution in Syria is widespread, that most of the cases are in boys in the first decade of life, that the stones are usually solitary, and that they are not due to congenital malformations of the bladder neck.

The diagnosis of bladder stone in children usually presents no difficulties. The history is very characteristic. The Syrian

parent may state the correct diagnosis in answer to the doctor's first question. The child micturates often, and he cries out with pain during the act. He grasps the glans penis. The stream may be interrupted suddenly. Occasionally there is a constant dribbling of urine from a full bladder; but this usually means that the stone is in the urethra. Priapism is a common symptom.

Physical examination gives little diagnostic information. One may find only excoriation of the penis.

The urine is usually clear, but it contains albumin and a few white blood cells. Gross pyuria is infrequent. Red blood cells were found in the urine in only four of thirteen cases. Gross hematuria seems to be a rare finding in this condition; in our series, it occurred only in the case of ureteral calculus.

Special diagnostic procedures, such as palpation by rectum or cystoscopic examination, may be used to prove the diagnosis. The simplest sure method is the passage of a small sound. X-ray examination is preferred because it is painless and does not traumatize. The stones can be visualized even when they are relatively radiotransparent, if the proper exposure is used. (Figs. 1, 2, and 3.)

The operation of crushing a bladder stone by means of a lithotrite which is passed through the urethra is successfully used by some operators. Any great disproportion between the size of the calculus and the size of the urethra requires cystotomy. Many Syrian peasants think that sterility is a late complication of the disease. This was a factor in leading us to avoid urethral instrumentation. Our cases were all treated by suprapubic cystotomy.

Little or no preoperative treatment is needed, as the urine is usually clean. The boy is kept in the hospital for at least

\* Grateful acknowledgment is made of the help of Dr. Abdul Lateef Bisar, Dr. Harry Boyes, and Dr. Waheeb Nini of Tripoli, Dr. Ellis H. Hudson of Deir ez Zore, Dr. Herbert Torrance of Tiberias, and Dr. Ernest Wyder of Nazareth.

twenty-four hours before operation and methenamine is given by mouth.

A general anesthetic is required. Ether

bladder well, for the operation involves far less trauma when there is no necessity of searching for the bladder.



FIG. 1. Age  $2\frac{1}{2}$  years. The x-ray picture suggested that the stone was in the urethra. It was found in the bladder.

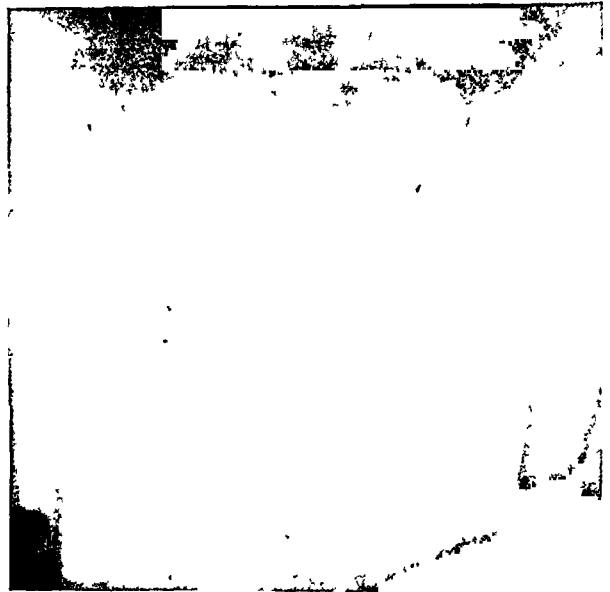


FIG. 2. Age 2 years. The stone shadow is seen superimposed upon the coccyx.

and oil administered by rectum is very satisfactory when the dosage is accurately computed on the basis of body weight.

The bladder is distended with sterile water or some suitable solution, such as boric acid. Catheterization is not necessary. Using an aseptic technique, the nozzle of an ordinary large syringe is introduced

A midline suprapubic incision is made. Care is taken not to separate the layers of the abdominal wall any more than is necessary, as all the tissues exposed will be contaminated with diluted urine. The

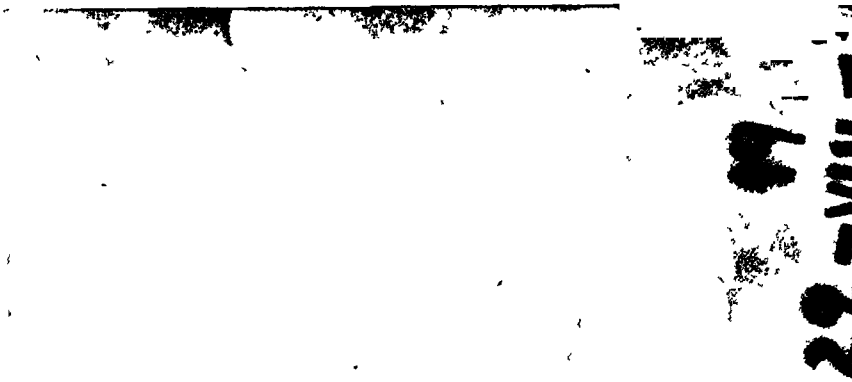


FIG. 3. Age 6 years. The stone shadow is situated above the symphysis pubis. The large eccentric nucleus shows clearly.

into the external meatus, and fluid is slowly injected until the bladder is a visible abdominal tumor. If the fluid is expelled, more anesthetic may be needed. One should not hesitate to distend the

peritoneal reflection should be identified and avoided. The bladder is secured by guy sutures and opened by a stab wound which is extended laterally. The fluid is sucked out and the bladder is explored gently. The

stone is removed either with forceps or spoon. Stone forceps with spoonlike blades are convenient, but not at all indispensable.

operative field by the assistant's finger in the rectum.

The wound in the bladder is closed

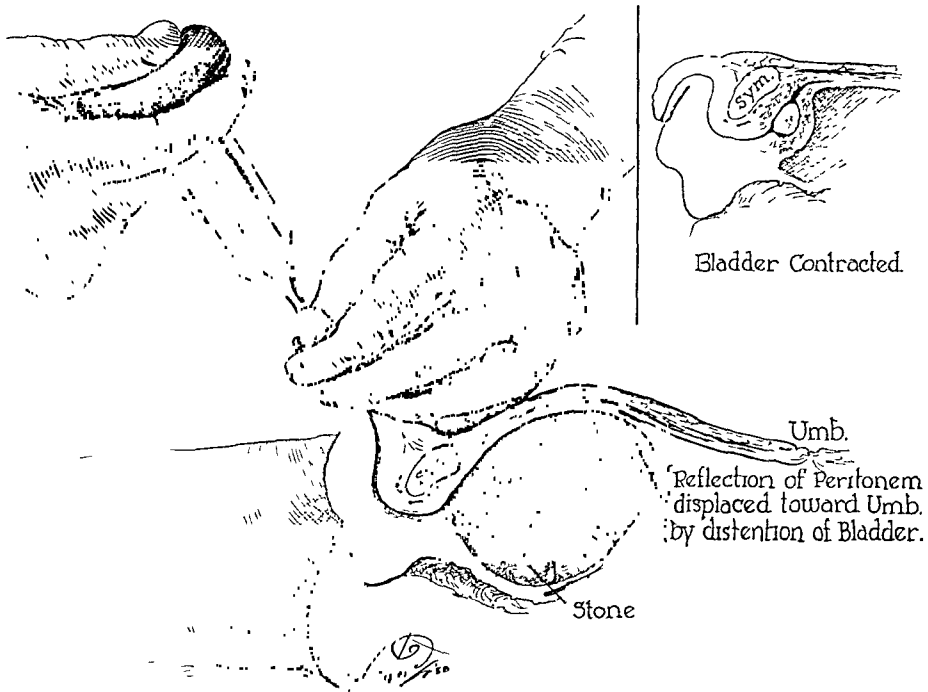


FIG. 4.

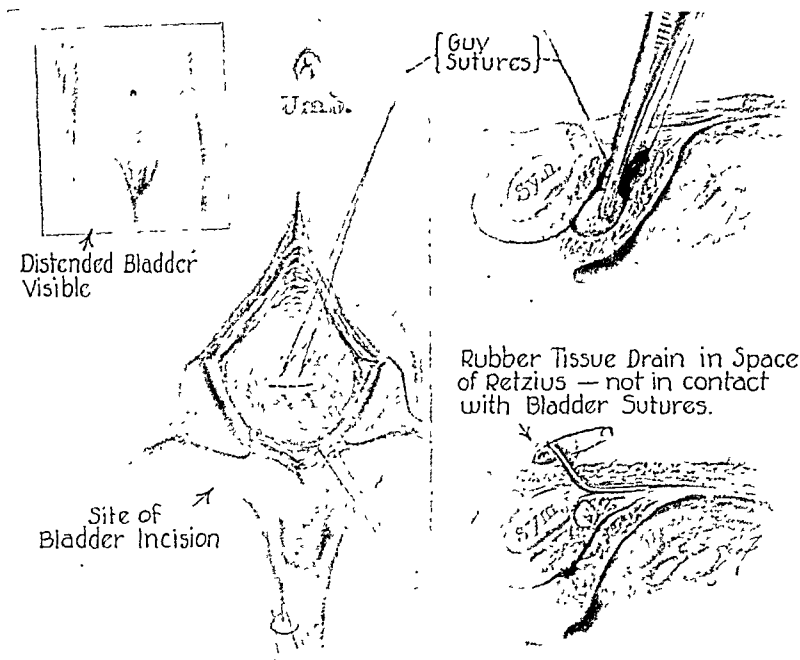


FIG. 5.

When the stone lies deep in the neck of the bladder, it may be delivered into the snugly with a continuous stitch of plain catgut in the muscularis. The mucosal

layer is never stitched, because the presence of suture material in or near the bladder cavity tends to cause recurrence of stone. If the wound is small, it may be closed with a purse-string suture. A second line of suture may be used to invert the first, but, if the stitches are properly placed, one continuous suture is sufficient. The continuous stitch is better than interrupted stitches in the bladder because it tends to shorten the wound when it is drawn tight, and because it reduces knots to a minimum.

The wound is irrigated with warm saline solution. A small rubber tissue drain is left in the prevesical space, preferably not directly to the site of suture of the bladder. The abdominal wall is closed in layers, using fine chromic catgut in the anterior sheath of the rectus muscle.

No indwelling catheter is used. Soon after the child awakes from anesthesia, he micturates normally and is pleased to find that the act is painless.

The wound heals by primary intention. There is some reaction about the incision, redness and swelling, due to contamination with diluted urine at the time of operation, but no pus forms if ordinary precautions have been taken and the bladder sutures are competent. The drain is removed on the second or third day.

If the closure of the bladder is not tight, urine escapes about the drain and the dressings are soaked. In such a case, it is wise to remove all the stitches in the abdominal wall at once, and leave the wound open, to heal eventually by granulation. The convalescence is prolonged, but the end result may seem just as good as if primary union had occurred.

When there is pyuria with bladder stone in children, the condition may be grave,

because this often means bilateral pyonephrosis. The patient should be carefully prepared for operation by rest, large amounts of fluids and medication. The bladder should be irrigated before operation. A suprapubic catheter should always be employed in the presence of pyuria.

The results of the operation are almost uniformly satisfactory, as reported to us by various surgeons in Syria. Only one recurrence has come to attention. In our own short series, there were no recorded recurrences and no deaths. One child was taken from the hospital in very poor condition; but there were subsequent reports that he recovered.

#### SUMMARY

1. Solitary urinary bladder stones in small boys are not uncommon in Syria.
2. A characteristic dysuria with interruptions suggests the diagnosis. X-ray or sounding proves it.
3. Most of the patients have relatively clean urine. Cystitis does not seem to be a marked feature of the disease.
4. Uncomplicated cases are treated by suprapubic cystotomy with immediate closure and without the use of a catheter.

#### REFERENCES

1. CAMPBELL, M. F. Urinary calculi in infancy and childhood. *J. A. M. A.*, 94: 1753, 1930.
2. COLLINS, A. N. Urinary lithiasis in infancy. *Am. J. Dis. Child.*, 6: 245, 1913.
3. JOLY, J. S. Stone and Calculous Disease of the Urinary Organs. London, 1929. Wm. Heinemann.
4. MCCARRISON, R. A lecture on the causation of stone in India. *Brit. M. J.*, 1: 1009, 1931.
5. THOMAS, G. J., and TANNER, C. O. Urinary lithiasis in children. *J. Urol.*, 8: 171, 1922.
6. THOMSON, J. O. Urinary calculus at the Canton Hospital, Canton, China. *Surg., Gynec. & Obst.*, 32: 44, 1921.



# LYMPHOSARCOMA OF THE MAMMARY GLAND\*

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A DEFINITE surgical axiom that masses in the breast should always arouse suspicion of carcinoma and be investigated is now fairly well established. Of the malignant changes that may be found in such nodules, adenocarcinoma is of course the most frequent. Sarcoma occurs much less frequently. There are also conditions in which the appearance of a mass in the mammary gland is the first sign of a systemic neoplastic process. Such cases must be differentiated from those of adenocarcinoma in order that appropriate treatment may be started. These systemic conditions include chloroma, with and without accompanying blood changes, lymphatic leucemia, lymphogranuloma of the Hodgkin type and lymphosarcoma. The two latter conditions may be either disseminated or sharply localized to the breast. To clarify the pathologic changes that may be associated with such nodules in the mammary gland, the collected cases have been reviewed. In general, three types of growth may be found: (1) those in which involvement of the gland is merely part of a widespread generalized process; (2) the less frequently appearing cases of an apparently localized lymphogranulomatous neoplasm which is subsequently found to be but a part of a systemic disease; and (3) localized lymphogranuloma and lymphosarcoma.

A small number of cases of chloroma in which the breast has been involved have been reported. The hematologic picture associated with this pathologic change is not constant.

Lymphatic and myeloid types of leucemia may be found or there may be no blood changes. The chief significance of

chloroma is that it denotes a process of pronounced malignancy no matter what the blood may show. Of the seven cases of chloroma collected, blood examination was not done in two cases (Sheild and Earle), while in a third (Huber), it was done only after death. At this time, there was a considerable increase in leucocytes that resembled the cells found in the tumors.

Acute lymphatic leucemia accompanying the chloroma was reported by Trevithick and by Weinberger. Simon's patient is of particular interest in that she was thought to have a malignant tumor of the breast, perhaps a carcinoma, when she first presented herself. She was a 16 year old girl who had noted a small swelling in the left breast for about four weeks. Growth of the tumor was rapid and the entire mammary gland became involved. She had not suffered a loss of weight, although she was pale and ill. A large, hard, non-tender nodule, to which, in part, the skin was attached, was found in the left breast. Venous dilatation was present in the skin, but the tumor was movable on the pectoral muscle. A small node was present at the edge of the tumor and the axillary lymph nodes were involved. The spleen was not enlarged, but a palpable nodule was felt during the rectal examination. With malignancy in mind, a radical amputation of the breast was performed. On cross-section, the tumor and lymph nodes were green in color and this suggested a diagnosis of chloroma. The day following operation, examination of the blood revealed that the patient had an acute myeloid leucemia.

An associated increased leucocyte count was not present in Reid's patient, a 30

\* Abridgment of portion of thesis submitted by Dr. Miller to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

year old married woman who was admitted with complaints of vomiting, icterus and mammary tumors. She stated that five stricture of the common bile duct was performed. A biliary fistula subsequently developed. One month after the initial

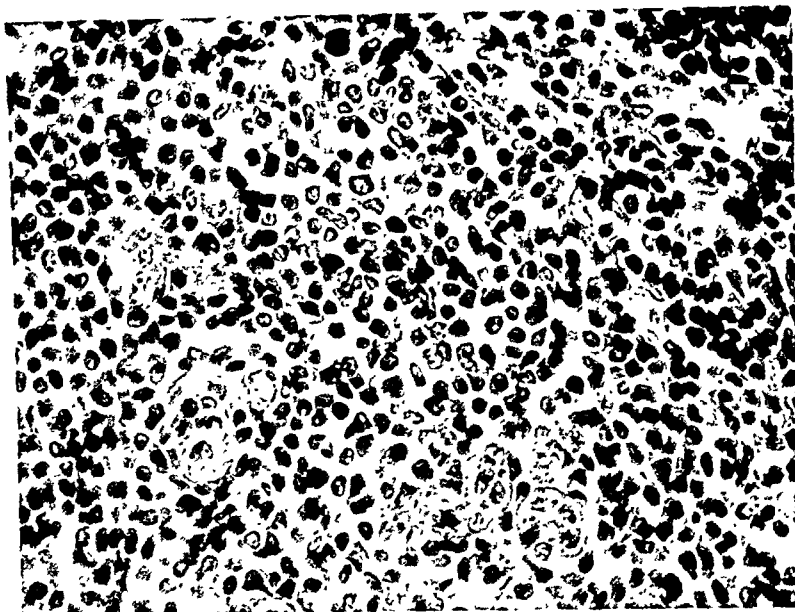


FIG. 1. Lymphosarcoma ( $\times 420$ ).

and a half months before admission, she had noted a small nodule in her left breast. This mass increased in size and she then found three small nodules in her right mammary gland. Both breasts were treated with radiotherapy for three months, with the left breast receiving most of the treatment. A good response in the left mammary gland was noted and the tumor almost disappeared but it was soon replaced by another in spite of the radiotherapeutic treatment. The right breast was uninfluenced by this therapy. Five months after the onset of the disease, nodules in the left axilla were noted. Icterus was present upon admission. With the exception of the nodes in the left axilla the superficial lymph nodes of the body were not enlarged and there was no increase in substernal dulness. Heart and lungs were normal but there was some tenderness in the gall-bladder region, and two leiomyomas were thought to be present in the uterus. The patient's leucocyte count at this time was 6,200 in each cubic millimeter of blood.

At the first operation, the right breast was removed and a choledochostomy for

operative procedures, the left mammary gland and axillary nodes were removed. A second white count the day after this operation was 7,500. The tumors in both breasts and the axillary lymph nodes were green. Two weeks before death, the patient's home physician found a tumor in the rectum which he considered a sarcoma. Death occurred nine months after the first appearance of the mammary tumors. This case is remarkable, for the only objective evidence at first that the patient suffered from chloroma was the presence of the mammary neoplasms.

The breast may also be the seat of metastatic deposits in lymphatic leucemia without the presence of chloroma. Dencker's patient had a widespread dissemination of lymphatic cells and the mammary glands were almost replaced by neoplastic tissue. The white blood cell count was 710,000 per cu. mm., with 82 per cent small lymphocytes and 6 per cent large lymphocytes.

Similar to Reid's case, in which the first sign of disease was the appearance of a mammary tumor, are the cases of McWilliams and Hanes and of Haram. Two weeks



before admission, the patient of the former men noted a mass in the right breast which apparently was not growing. The opposite

breast was considered to be normal. Removal of the nodule and subsection to microscopic investigation revealed that a benign lymphoma was present. However, another mass appeared in the breast and then its mate became involved, all the tumors growing steadily. Both mammary glands were removed, first the right and then the left after an eight day interval. A diagnosis of lymphosarcoma of each breast with involvement of the right axillary lymph nodes was then made, but subsequently a lymphatic leucemia was discovered.

Haram has reported a similar case of lymphatic leucemia in which the only gross manifestations were in the breasts. The tumor removed from the left breast had a pathologic appearance simulating a sarcoma, with dense infiltration by large mononuclear cells. Five months later, a tumor of the same structure was removed from the right mammary gland. Examination of a blood film at the time of the first surgical procedure showed no abnor-

malities, but after the second operation the white blood count was 17,800, 99.5 per cent being lymphocytes.

Schultz, in the handbook of Lubarsch and Henke, gave details about two patients who had a widespread lymphogranuloma in which both breasts were infiltrated. Microscopic examination of the tissue from the first patient revealed a typical picture of Hodgkin's disease with lymphocytes, eosinophiles, Sternberg giant cells and much connective tissue. Generalized involvement was also present in the other case, but Sternberg cells and eosinophiles were not part of the microscopic picture of the lymphogranuloma. Schultz also included a case from the Vienna Pathological Institute in which the patient had a dissemination which was again widespread. Lymphocytes, Sternberg cells and new connective tissue were the prominent microscopic features of the tumor tissue.

Lymphogranuloma has appeared as an isolated tumor, as in the case of Kückens. A 16 year old girl had a mass in her right breast for several weeks. This was treated conservatively, but owing to an increase

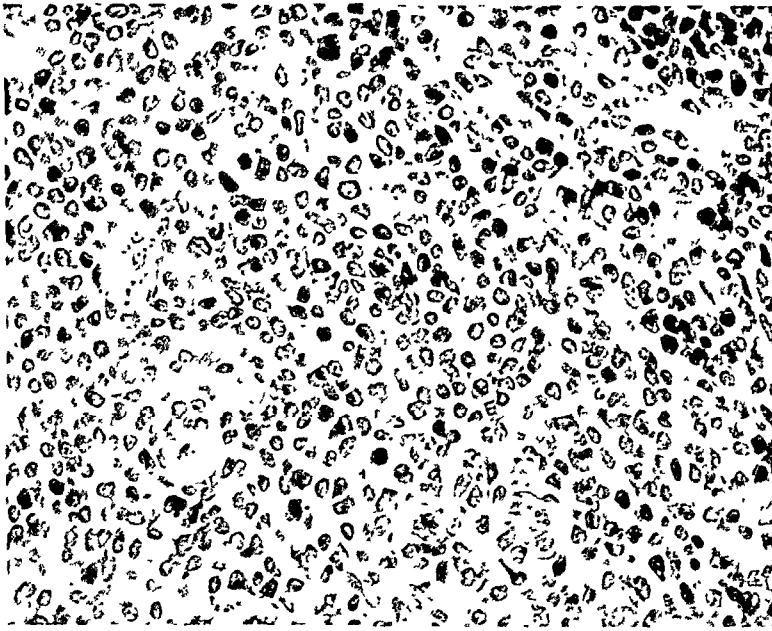


FIG. 2. Lymphosarcoma ( $\times 130$ ). Note closely packed areas of malignant cells.

in size, the thought that it might be a malignant lesion became more prominent. The neoplasm had no connection with the patient received Roentgen treatment for twelve months, and four months later (sixteen months after operation), a tumor

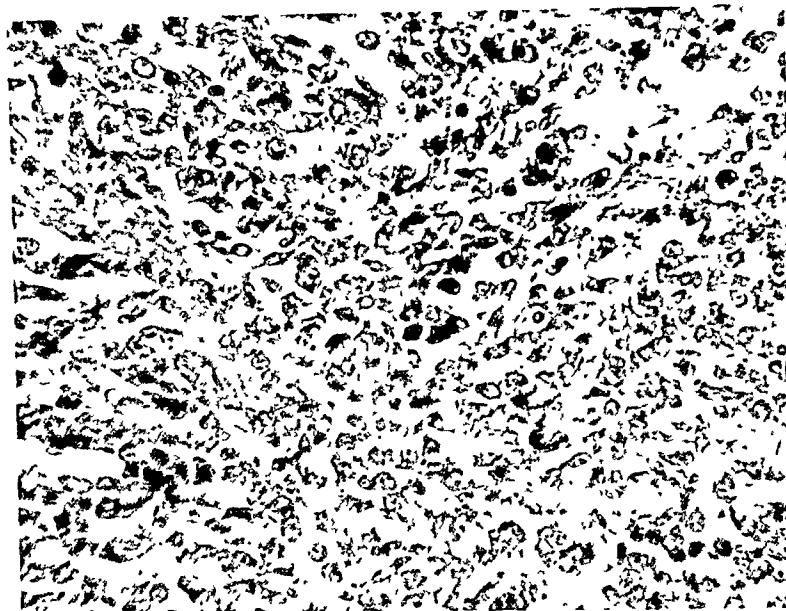


FIG. 3. Enlargement of Figure 2. The malignant cells are of "medium" size.

ribs or intercostal spaces, there was no enlargement of the cervical, inguinal or abdominal lymph nodes and the spleen was not enlarged. At operation, the right breast and underlying muscles were found to be infiltrated with a grayish-white hyperplastic tissue which upon microscopic examination was found to be richly cellular and remarkable for the high content of eosinophilic leucocytes. Moderately numerous small foci of necrosis and proliferation of connective tissue cells and Sternberg giant cells were also present.

Somewhat similar is the patient of Risak. This 67 year old married woman had noted a swelling in her right axilla for three months. The right nipple was retracted and, after a diagnosis of mammary carcinoma had been made, a radical amputation was done. The breast showed a "chronic cystic mastitis," but the lymph nodes which had extended into the mammary tissue were involved by a lymphogranulomatous process. No mention was made of blood changes and no microscopic description of the lesion was given. Kreibitz has added some details to this case. The

was noted in the left breast and there was enlargement of the left axillary lymph nodes. The spleen was slightly enlarged. Further Roentgen treatment caused a disappearance of the infiltration.

Lymphosarcoma, as part of a generalized process, has been described by Kundrat and by Schoen. The former discussed the case of a 38 year old woman from Störk's clinic in which the outer half of the left breast had been removed, apparently for carcinoma. However, there was widespread involvement of the body and both breasts at a later date. Schoen also noted that both breasts were involved in a case of lymphosarcoma in a 39 year old man with gynecomastia. Amputation of the left breast because of a tumor thought to be carcinoma was described by Ghon and Roman in a 44 year old married woman, who was later discovered to have a lymphosarcoma of the anterior mediastinum which became widespread. Elsberg briefly referred to a patient in whom multiple tumors developed in both breasts. A simultaneous radical amputation was done, and a diagnosis of round-cell sarcoma

of the lymphosarcoma type was made. The mammary glands but not the axillary lymph nodes were involved.

Somewhat more unusual is the patient of Judson, who was thought to have a carcinoma of the left breast with axillary metastasis. After radical amputation, an adenocarcinoma of the mammary gland was reported, but the lymph nodes were considered to be involved by a benign lymphoma. However, recurrences of tumors in the submaxillary region, the tonsil and other regions occurred and this patient too was discovered to have a lymphosarcoma.

#### REPORT OF CASES

Two lymphosarcomas in which the mammary gland has been involved have been observed at The Mayo Clinic.

**CASE I.** The first occurred in a 28 year old white married woman with a negative family history of malignant lesions, who complained of weakness of a year's duration, palpitation, nausea and vomiting, which were most frequent at the time of her periods, and headache. The latter had been present for eight to ten years and originated in the frontal region, then extending to the occipital region. The patient's appetite had been fair and she had not lost any weight.

Upon physical examination, a large nodular mass was found in the upper lateral portion of the right breast and a second smaller nodule in the left mammary gland, with a palpable lymph node present in each axilla. The heart and lungs were considered normal. Blood pressure was 135/80. Some abdominal tenderness was present. The concentration of hemoglobin (Dare) was 76 per cent, the erythrocytes numbered 4,700,000 and the leukocytes 3,200 in each cubic millimeter of blood. Wassermann reaction was negative. Roentgenographic examination of the chest revealed an old calcification of the upper lobe and apex of the right lung, which was suggestive of an old tuberculous lesion.

At the time of operation, a hard nodule in the upper quadrant of the right breast was removed and after pathologic examination, a radical amputation was performed. Multiple foci of lymphosarcoma, the largest 5 cm. in diameter and the smallest 1 cm. in diameter,

were present. The axillary lymph nodes were not involved. Removal of a nodule from the left breast at the same time revealed a similar type of malignant deviation 2 cm. in diameter. A subsequent roentgenogram of the chest revealed a mediastinal mass not attached to the aorta. After a course of radiotherapy an ulceration subsequently developed at the base of the tongue and epiglottis which filled up the sulcus in this locality. There was some edema of the arytenoid muscles and the aryepiglottic folds with ulceration. It was suggested that this process might be either part of the lymphosarcomatosis or possibly a primary infection. The patient became worse and died a little more than seven weeks after she was first seen.

Under the microscope, the portion of the mammary gland affected was seen to be very cellular and nothing of the structure characteristic of breast tissue remained. (Fig. 1.) The stroma was small in amount and eosinophilic, with blood vessels relatively few in number. The amount of cytoplasm in the individual cells was small, dark staining nuclei occupying the major portion of the cell. The nuclei were both anisocytotic and poikilocytotic, and the chromatin material was granular and uniformly distributed throughout the nuclear body. Many prominent nucleoli and a few mitoses were seen. The pathologic picture was that of lymphosarcoma.

**CASE II.** Somewhat more unusual is the second case. A 38 year old married woman stated upon admission that she had noted a lump in her breast for ten days. There was no family history of malignant lesions. There had been no discharge from the nipple, and no loss of weight or strength. The patient was moderately obese. Enlargement of the superficial lymph nodes could not be demonstrated. A small nodule was found in the lower part of each lobe of the thyroid. In the left breast a firm movable nodule about 3 cm. in diameter was found, with the skin overlying the mass retracted, but the nipple normal. Pathologic changes were not demonstrable in the right breast. A soft systolic murmur was heard all over the precordium, but the lungs were clear and resonant throughout. The abdomen was normal. A large fibroid uterus was discovered upon bimanual examination.

The hemoglobin was 12.9 Gm. per 100 c.c.; erythrocytes numbered 4,100,000 and leuco-

cytes 6,300. The results of roentgenographic examination of the chest were normal.

The tumor was excised and after the pathologic report, the operation was completed as a radical procedure. An uneventful convalescence followed. Upon leaving the hospital, the patient was given a course of Roentgen therapy and advised to have a second course in a month. Upon her return about four months later, no evidence of recurrence was found and a hysterectomy was carried out. This patient was well and without return of her malignant lesion six years after her operation.

The microscopic examination of the tissue removed from the breast was all the more interesting in the light of the patient's postoperative course. An extremely cellular structure without definite arrangement could be seen under the microscope. (Figs. 2 and 3.) Nothing suggestive of the mammary gland was present; the glandular tissue had been replaced by tumor tissue. Under oil immersion, the neoplastic cells were seen to be manifestly malignant and contained a little cytoplasm eosinophilic in nature. The nuclei were hyperchromatic and irregular in size and shape. Many were large and clear staining with prominent nucleoli, and some were of horseshoe shape. However, the cells were not of the Sternberg type, and eosinophiles and plasma cells were absent. Many mitotic figures, a scanty stroma and a small number of thin walled blood vessels are seen. The picture was that of a malignant lymphosarcoma.

The explanation for the presence of a primary lymphosarcoma of the breast is rather difficult since lymph follicles are not ordinarily located there, but the following suggestion may be made. Large collections of lymphocytes are found in the mammary gland in most chronic pathologic entities affecting the breast. Secondary lymph follicles may be formed and a continuation of the stimulus, whatever it is, may produce a malignant change. Although difficult to explain, an excellent result has been achieved in Case II. This patient represents a rare case of a "five-year cure."

In both cases presented, the diagnosis was not and could not have been made until operation, for differential diagnosis from carcinoma rested upon microscopic exami-

nation. However, in some of the cases reviewed, the diagnosis could have been reached by a routine preoperative examination of the blood. Every patient who has a mass in the breast upon which surgical intervention is contemplated, should have a careful physical examination and, besides the various necessary laboratory examinations, a leucocyte and differential count. The conditions falling into the various categories described previously will be recognized and appropriately treated. Where blood changes are not present, the tumor in the breast should be removed and, if a lymphogranuloma or a lymphosarcoma is found, radiotherapy should be instituted.

#### SUMMARY

The collected cases of lymphosarcoma of the mammary gland have been reviewed and three types of growth described. Accompanying blood changes of significant character are sometimes present and should not be overlooked before operation is undertaken. Evidence of lymphosarcomatosis may at first be only found in the breast, later to appear in other localities (Case I), but it may also be primary in the mammary gland (Case II). These case histories are given in detail and their surgical treatment is presented.

#### REFERENCES

1. DENCKER, CHRISTIAN. A case of extensive leukemic infiltration of the mammary gland and skin. *J. A. M. A.*, 56: 417, 1911.
2. EARLE, HENRY. A case of diseased testicle, accompanied with disease of the lungs and brain, and terminating fatally. (Communicated by Lawrence, William.) *Tr. Med.-Chir. Soc. London*, 3: 59, 1812.
3. ELSBERG, C. A. Multiple lymphosarcoma of both breasts. *Ann. Surg.*, 60: 767, 1914.
4. GHON, A., and ROMAN, B. Über das Lymphosarkom. *Frankfurt. Ztschr. f. Path.*, 1: 138, 1916.
5. HARAM, B. Lymphatic leukaemia with bilateral mammary changes: report of a case. *Lancet*, 1: 1277, 1937.
6. HUBER, KARL. Studien über das sogenannte Chlorom. *Arch. f. Heilk.*, 19: 129, 1878.
7. JUDSON, H. A. Simultaneous lymphosarcomatosis and carcinoma of the breast in the same individual. *Radiology*, 29: 578, 1937.

8. KREIBIG. Discussion. *Zentralbl. f. allg. Path. u. path. Anat.*, 54: 109, 1932.
9. KÜCKENS, HANS. Ein lokales Lymphogranulom der Brust in Form eines Mammatumors. *Beitr. z. path. Anat. u. z. allg. Path.*, 80: 135, 1928.
10. KUNDRAT. Ueber Lympho-Sarkomatosis. *Wien. klin. Wchnschr.*, 6: 211, 234, 1893.
11. MCWILLIAMS, C. A., and HANES, F. M. Leukemic tumors of the breast mistaken for lymphosarcoma. *Am. J. M. Sc.*, 143: 518, 1912.
12. REID, MONT. Ueber ein doppelseitiges myeloides Chlorom der Mamma. *Beitr. z. klin. Chir.*, 95: 47, 1914.
13. RISKA. Über zwei seltene Erkrankungen der weiblichen Brustdrüse. *Zentralbl. f. Chir.*, 56: 403, 1929.
14. SCHOEN, RUDOLF. Lymphosarkomatose mit Beteiligung der Brüste bei einem Gynakomsten. *Frankfurt. Ztschr. f. Path.*, 25: 112, 1921.
15. SCHULTZ, A. Pathologische Anatomie der Brustdrüse. In Lubarsch, O., und Henke, F. *Handbuch der speziellen pathologischen Anatomie und Histologie*. Berlin, 1933. Julius Springer, vol. 7, pt. 2, pp. 1-208.
16. SHEILD, A. M. A Clinical Treatise on Diseases of the Breast. London, 1898. Macmillan.
17. SIMON, W. V. Myeloische Chloro-Leukämie (Chlorom) unter dem Bilde eines malignen Mammatumors. *Berlin. klin. Wchnschr.*, 1: 893, 1912.
18. TREVITHICK, EDGAR. A case of chloroma, with clinical history and account of post-mortem appearances. *Lancet*, 2: 158, 1903.
19. WEINBERGER, M. Ueber lymphoides und myeloides Chlorom, sowie dessen Beziehungen zur lymphoiden und myeloiden Leukämie. *Ztschr. f. Heilk.*, vol. 28, 1907. *Abt. f. inn. Med.*, 1-97.



IN cases of senile arteritis, at the earliest possible moment I do a periarterial sympathectomy, an arteriectomy, or a lumbar sympathectomy according to the particular case. In this way it is possible to relieve almost all elderly sufferers from senile arteritis, if a general examination shows that they have no uremic or glycemie conditions which contra-indicate operation.

From—"Surgery of Pain" by René Leriche (Williams and Wilkins).

# BENIGN UTERINE HEMORRHAGE IN NONPREGNANT WOMEN

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UTERINE bleedings in the non-pregnant woman which are not the result of malignant tumors are commonly called benign hemorrhages. The term is a misnomer, since hemorrhage is, per se, an evidence of some abnormal process and cannot be benign. Hence the use of these two words as appositives is manifestly erroneous. However, it is common medical usage, and is generally understood to mean hemorrhage from causes other than malignant growths.

The subject is a very large one and perforce can only be reviewed in a somewhat cursory fashion in a communication such as the present one.

## BLEEDING IN EARLY LIFE

Bleeding from the female genitalia of pathologic origin may occur at any time from birth to the last day on earth of the oldest woman; and because of this it is convenient to divide genital hemorrhage into several age groups, corresponding to the various physiologic cycles of the organs of reproduction. During infancy and childhood genital hemorrhage may be due to:

Precocious menstruation.

Nongenital hemorrhage of the newborn.

Malignant tumors of the lower genital tract (sarcoma botryoides).

Rarely, bleeding from violent inflammation of the mucosa in gonorrheal vulvovaginitis.

Precocious menstruation is seldom seen, there being but a few hundred cases in the literature. (Lenz was able to collect only 130 cases from 1680 to 1913.)

In some instances where the precocity is not extreme, the phenomenon may be due to some individual variation in the responsible endocrine mechanism; but where menstruation occurs at a very early age, the cause is usually some definite

lesion in one of the ductless glands. The rare granulosa cell tumor of the ovary is a recognized cause. These malignant growths are follicular in their structure, and hence can readily stimulate the infantile endometrium to a point of bleeding comparable to menstruation.

Sarcoma of the ovary, large cysts, and teratomata have also been reported as causative. Tumors of the suprarenal gland, the pineal may be factors. Indeed, as Novak says, it is rare not to find a tumor of one of the endocrine organs in cases of menstrual precocity of extreme grade.

In some of these interesting cases the catamenia continues steadily from its early onset to the menopause. In most, however, it is regular for a while and then ceases, to recur again at the usual age of puberty.

Nongenital hemorrhage of the newborn is bleeding, rarely massive, often only discovered by the presence of blood cells in the microscopic examination of vaginal smears. It is probably due to the sudden withdrawal of estrin from the fetal circulation after delivery.

The uncommon finding of grape-like masses of sarcomatous tissue filling the vagina of infants will explain the bleeding from this cause. Occasionally vulvovaginitis due to an especially virulent strain of the gonococcus produces a violent inflammatory reaction in the vaginal mucosa with more or less bleeding.

All in all, genital hemorrhage in infants and young girls is uncommon, and each case requires most careful study to determine the etiologic factors involved.

## BLEEDING IN YOUNG ADULTS

*Hemorrhage in young adults may be caused by:*

Systemic disease.

Malignant tumors of the corpus or cervix uteri.

Adnexal inflammatory disease.

Polyps of the cervix or corpus uteri.

Endocrine unbalance, "the hemorrhage of adolescence," "functional hemorrhage."

The bleeding may take the form of menorrhagia or metrorrhagia. Usually the former is the functional variety while the latter is characteristic of inflammatory lesion, polyp or neoplasm formation.

Systemic disease is far more prone to lead to amenorrhea or oligomenorrhea than to excessive menstruation; but syphilis is sometimes responsible for profuse hemorrhage, while chronic valvular heart disease is a definite cause. The anemias, tuberculosis, etc., do not often tend to excessive menstruation. Malignant tumors of the uterus, while uncommon in young women, are being reported with increasing frequency—as witness a girl now under the care of the writer, who at the age of 22 is suffering from a far advanced epidermoid carcinoma of the cervix which bled so freely as to cause a profound anemia.

Adnexal inflammation as a cause of metrorrhagia and menorrhagia is often overlooked. Bécclère<sup>1</sup> has observed in four years sixty-five cases of functional uterine bleeding due to genital infection, most often caused by the gonococcus. This author believes that the bleeding is due to a secondary ovarian dysfunction.

Every active gynecologist has observed young women patients in whom irregular, sometimes profuse, uterine hemorrhage, together with other pelvic symptoms, led to the diagnosis of extrauterine pregnancy, but in whom laparotomy disclosed a subacute salpingitis.

Uterine or cervical polyps, too, are not common in young women, but may occur; and when present, disclose their usual tendency to irregular small hemorrhages often induced by exertion, coitus, douching and so on.

Endocrine unbalance is probably the most common variety of menstrual bleeding noted in young girls. This so-called

functional bleeding may occur at any period during the cycle of reproductive life. Büttner, Novak<sup>2</sup> and others feel that it is most common during middle life, after 40, the proportion varying from 51 per cent to 77 per cent of the total number in various groups of statistics.

Functional hemorrhage during puberty and early adolescence forms but a small fraction of the whole number of cases, usually stated as accounting for from 5 to 10 per cent, but in the experience of the writer even this proportion is too high, 2 or 3 per cent seeming to be nearer the truth.

The whole subject of functional hemorrhage is still in a state of flux, students of this phenomenon varying widely in their interpretation of its mechanism. It has been widely accepted that functional uterine bleeding is almost invariably associated with endometrial hyperplasia, and this concept is responsible for the corollary view that, if the hyperplastic endometrium can be converted into the secretory phase, bleeding will cease. This is the basis of endocrine therapy, some form of the luteinizing hormone being utilized to bring about a secretory phase.

Recent study, however, has demonstrated to the satisfaction of an increasing number of investigators that the relationship of bleeding to endometrial hyperplasia is by no means a constant one, and that many exceptions are found to it. Payne<sup>3</sup> studied the clinical records of 534 patients with endometrial hyperplasia in the effort to determine its rôle in uterine hemorrhage at various ages. Abnormal bleeding was present in only 85 per cent of the premenopausal hyperplasias. Payne concludes that just as hyperplasia may occur without abnormal bleeding, so may abnormal bleeding occur without hyperplasia. In approximately two-thirds of the cases of functional uterine hemorrhage endometria were obtained which were devoid of hyperplasia.

Jones<sup>4</sup> found that in eighty-three consecutive cases about 14 per cent were

associated with secretory endometrium. He studied in detail forty-one cases of functional uterine bleeding in which secretory endometrium was found. Greenhill, in his editorial comments in the Year Book of Obstetrics and Gynecology, emphasizes the fact that almost any type of endometrium may be found in these cases, which, he believes, is the reason that response to treatment is so variable. A series of cases now being studied at Kensington Hospital for Women by the writer and his associates seems to indicate that in the climacteric and postclimacteric bleedings atrophic endometrium, almost aglandular, is far more common than any other variety.

#### BLEEDING DURING MIDDLE LIFE

Bleeding during the middle decades of life may be due to:

Functional causes.

Benign neoplasms mostly fibromyomata.

Malignant neoplasms.

Endometriosis, endocervicitis, polyps and adnexal disease.

Hypertensive cardiorenal disease.

In the middle years, say from 35 to 55, uterine hemorrhage has a greater variety of causative agents than obtains either during youth or in old age. Here the benign tumors play a most important part, and endo-cervicitis with erosion following the traumatism of parturition is often responsible for bleeding. Cancer of the fundus as well as the cervix is all too common a factor.

An interesting analysis of the records of patients suffering from uterine hemorrhage, excluding all those cases in which pregnancy was a factor, has been published by Weintraub,<sup>5</sup> who found that in 4,421 admissions on the gynecologic service of a general hospital, 738 patients, or 16.6 per cent of the whole number, complained of abnormal uterine bleeding not associated with pregnancy.

Of these 738 patients, the bleeding was due to:

Fibroid tumors in 340 (46 per cent).

Endometrial hyperplasia in 175 (23.7 per cent).

Fibrosis uteri in 68 (9.2 per cent).

Non-malignant polyps in 49 (6.6 per cent).

Malignant neoplasm—cervix and corpus in 28 (3.7 per cent).

Chronic pelvic inflammatory disease in 24 (3.2 per cent).

Benign ovarian neoplasm in 18 (2.4 per cent).

Anatomic displacements in 29 (3.9 per cent).

Undetermined origin in four patients.

This ratio agrees with that generally observed except in the very low incidence of carcinoma uteri. Weintraub explains this in part by citing the well-known comparative immunity to cervical cancer enjoyed by Jewish women. It may also be true that in the locality in which this hospital was situated, most cancer patients are cared for in special institutions. Certainly, speaking generally, carcinoma would account for far more than 4 per cent of a series of patients suffering from uterine hemorrhage.

The hemorrhage resulting from the presence of uterine fibroids depends much upon the mechanism of tumor growth. In those of the centrifugal type, whose growth tends away from the uterine cavity and toward the serosa, hemorrhage either is negligible, or continues to decrease as the tumor grows away from the center.

In centripetally growing tumors, on the other hand, the blood tends to increase steadily as the growth impinges more and more upon the uterine cavity, bringing the opposite endometrial surfaces together with sufficient pressure to cause superficial necrosis of these surfaces with vessel rhexis.

The bleeding may be of either menorrhagic or metrorrhagic type, the former being more common at first, being succeeded by irregular or indeed, almost continuous hemorrhage in many instances.

Hemorrhage resulting from the presence of malignant neoplasms requires but little



discussion here. The slight but persistent spotting, with more and more profuse menstrual periods culminating in a sudden massive hemorrhage forms a picture all too well recognized by the gynecologist.

In corporeal carcinoma spotting is not so common, the bleeding only beginning when the growth is fairly well advanced and then developing as a steady flow.

Bleeding in the late decades of life, post-climacteric bleeding, may be caused by any of the foregoing lesions, with the addition of senile vaginitis, which often is responsible for slight to moderate hemorrhages.

#### THE DIAGNOSIS AND TREATMENT OF UTERINE HEMORRHAGES

The diagnosis of the cause of uterine bleeding should always be regarded as a matter of major importance, and no detail of examination should be omitted which may lead to a correct interpretation of the etiology.

Increasing knowledge of functional hemorrhage and its treatment by means of endocrine preparations has resulted in many unfortunate instances wherein patients presenting themselves with uterine bleeding have been cursorily examined, assumed to be suffering from functional hemorrhage, and managed by various dosages of various endocrine products. Many early uterine malignancies have been overlooked in this manner, and any active gynecologic clinic can report all too large numbers of late, far advanced cervical and corporeal carcinoma which have followed prolonged medical treatment without exhaustive efforts at excluding such malignant growths.

In the writer's hospital services no patient is treated upon an assumption of functional hemorrhage without a definite knowledge as to the histology of the endometrium, a knowledge gained by the examination of the entire endometrium as removed by the curette, or at least by the study of endometrial biopsy specimens.

The ordinary diagnostic measures should be utilized in arriving at a conclusion. The detailed history, the exclusion of nongenital, systemic causes of bleeding, the careful bimanual and speculum investigation, all go without saying. The same general statements may be made concerning treatment. Fibromyomas are to be managed by hysterectomy, myomectomy or radium and x-ray according to the requirements of the individual case. Malignant neoplasms are treated by surgery or irradiation, or both, as the case may be. Polyps are excised, pelvic inflammatory disease managed according to the usual plan.

#### FUNCTIONAL HEMORRHAGE

There remains to be considered the treatment of functional hemorrhage, which is still somewhat confused in the minds of many of us. The bleeding may be attacked from one of several avenues:

1. Conversion of an abnormal endometrium into a secretory phase of this structure.
2. Endocrine therapy not intended to affect the endometrium directly but to regulate a general endocrine unbalance.
3. Compression of blood vessel walls—by stimulations of uterine musculature, ergot, cotarmine chloride (stypticin), breast stimulation, etc.
4. Decreasing the blood coagulation time, moccasin venom, koagamin, cevitic acid and vitamin c.
5. Blood transfusion.
6. Surgery.

In the management of functional uterine bleeding, it is often necessary, first, to control the immediate hemorrhage, and then to institute measures designed to prevent its recurrence.

#### STIMULATION OF THE UTERINE MUSCLE

Uterine hemorrhage may sometimes be controlled by the exhibition of drugs which act by compression of the blood vessels, and for this purpose the newer oxytocic principles of ergot are valuable agents.

Preparations of this new alkaloid, ergonovine, are marketed under various proprietary names, and should be administered orally in small dosage ( $\frac{1}{320}$  gr.) every four hours for six or eight doses. These powerful preparations may not be used for a long time since gangrene of the extremities may follow their prolonged administration.

#### REDUCTION OF BLOOD COAGULATION TIME

Control of bleeding by shortening the clotting time has been employed for some time with more or less success. Parathyroid extract has been advocated, on the principle that its use increases the amount of calcium in the circulating blood.

Moccasin snake venom has also enjoyed a considerable popularity as a clotting agent, especially for its effect upon the lesser vessels and the arterioles. The venom in dilutions of 1:3000 may be given hypodermically daily for two weeks, 0.5 cm. being the initial dose, which is increased in two days to 1.0 cc. Local reaction may follow its use.

*Irradiation of the spleen* has been advised in the view that the blood platelets are increased by the x-ray. The writer has no experience with this method.

*Koagamin.* Recently Steinberg and Brown of the Research Foundation, Kensington Hospital for Women, presented their work on the reduction of clotting time with *koagamin*, an extract containing oxalic acid and possibly vitamin K. This preparation has been extensively used by the writer with signal success. The drug is given intravenously in a dose of 3 c.c., which is followed by 2 c.c. intramuscularly every four hours for two to four doses. Within fifteen minutes of administration the clotting is reduced, sometimes as much as 50 per cent, and the effect lasts for from eight to ten hours.

#### ENDOCRINE TREATMENT

This is probably the therapeutic measure in most widespread use at this time.

The preparations used are chorionic gonadotropic hormones, as for example, antuitrin S, A. P. L. or antophysin. More recently extracts made from the blood of pregnant mares, gonadin or gonadogen, have been employed, but since these substances are derived from horse serum a skin sensitivity test is requisite before use.

All of these gonadotropic agents probably act by producing atretic changes in the ovaries.

The dosage varies, but the chorionic hormones are usually exhibited in intramuscular injections of from 100 to 1000 rat units daily for two days.

In connection with the above therapy, the anemia which results from severe hemorrhage must be treated by the ordinary measures employed for this purpose. Blood transfusion is of the greatest value after massive blood loss, and may be followed by the administration of iron in its various forms, lextron, and so on.

Treatment to prevent recurrences of functional bleeding consists in trying first the effect of the gonadotropic hormone as described above, the injection being begun ten days before the expected menstrual period. When the bleeding begins, koagamin may be given. Should this therapy fail to control the periodic hemorrhages, more radical procedures become necessary, and either irradiation of the uterus and ovaries by radium or x-ray or hysterectomy must be seriously considered.

Radium treatment is a valuable measure in combating uterine hemorrhage, but is subject to several contraindications. Radium may not be used in the presence of pelvic inflammatory disease, a series of cases of fatal peritonitis following such treatment being available in the literature.

In the opinion of the author, radium is not satisfactory, generally speaking, in the treatment of functional bleeding in women before the climacteric age. While it is theoretically possible so to regulate dosage that menstruation may be made to

cease for a predetermined period, later recurring, it is a fact that the individual response to radiation is extremely variable, and a complete menopause all too often follows what was intended as a purely temporary measure.

Furthermore, it seems true that radiation menopause in younger women is productive of more violent and prolonged nervous disorder than that following surgical castration.

The same objections hold for x-ray termination of ovarian function. After the climacteric age, however, radium and x-ray are measures of the greatest value, and may be employed without hesitation upon the proper indications.

Hysterectomy, with or without removal of the ovaries, may be necessary occa-

sionally. Needless to say, this is a somewhat radical treatment, but often produces a gratifying end result.

Time does not suffice for a discussion of the adjuvant measures utilized in the management of uterine bleeding. The discovery and control of associated pathologic conditions, proper maintenance of nutrition, elimination of psychic disturbances, and the like—all of these are necessary details if a bleeding woman is to be restored to normal health.

#### REFERENCES

1. BÉCLÈRE. *Bull. Soc. gynec et obst.*, 27: 507, 1938.
2. NOVAK, E. *Curtis Obst. & Gyn. Phila.*, 1933. Saunders, 1: 126.
3. PAYNE, F. L. *Am. J. Obst. & Gynec.* 36: 302, 1938.
4. JONES, H. W. *Am. J. Obst. & Gynec.* 35: 64, 1938.
5. WEINTRAUB, F. *Am. J. Obst. & Gynec.* 36: 476, 1938.



# ACTIVE IMMUNIZATION AGAINST TETANUS BY THE COMBINED SUBCUTANEOUS AND INTRANASAL ROUTES

## A SIMPLE PROCEDURE FOR THE MAINTENANCE OF A PROTECTIVE ANTITOXIN TITER

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ACTIVE immunization against tetanus is regarded by many as a safe and efficacious procedure.<sup>1-10</sup> It requires the injection of a primary course of two doses of alum precipitated tetanus toxoid or three doses of plain toxoid, which confers a basic immunity, to be followed by the injection of a "repeat" dose of toxoid whenever an injury occurs.

The repeated injection of toxoid immediately raises the question of sensitization. Another question of importance is the rate of antitoxin production following the injection of the repeat doses of toxoid. Finally, although local reactions at the site of injection are slight to moderate in severity, any procedure that requires the repeated use of "the needle" with subsequent sore arms is likely to meet with objections on the part of the patient.

The intranasal route has been successfully used for the administration of drugs, glandular extracts and various biological products.<sup>11-18</sup> Lesne et al.,<sup>23</sup> Salviolo,<sup>24</sup> Jensen,<sup>25</sup> Bousfield and King-Brown,<sup>26</sup> and more recently Wenger, Hampil and Masucci,<sup>27</sup> have reported on the use of diphtheria toxoid intranasally. Ramon and Zoeller<sup>19-22</sup> have also reported on intranasal immunization against diphtheria, tetanus, scarlet fever, and bacillary dysentery through the use of single or combined antigens. In 1927, these authors called attention to the chief benefits to be derived from the intranasal method of immunization, particularly with reference to diphtheria. These are simplicity of administration and absence of reactions. Thus, individuals that were strongly sensitive to diphtheria toxoid were immunized intranasally by Ramon with only a transient

swelling of the nasal mucosa. The chill, fever, malaise and local inflammatory swelling that usually follow the injection of diphtheria toxoid into sensitive adults were conspicuously absent. Ramon's objection to intranasal immunization was its expense, due to the need of three courses of treatment, each consisting of two daily instillations repeated for eight days. Each nasal treatment was equivalent to 0.5 c.c. of Ramon's toxoid.

Although systemic reactions are rarely encountered after the injection of tetanus toxoid we can definitely state from our experience with subjects that have been immunized against tetanus by the combined subcutaneous and intranasal routes that the instillation of toxoid into the nose rather than its injection under the skin is preferred by both adults and children.

We are interested particularly in the use of a product for the "repeat dose" that will not require subcutaneous injection and which will result in the development of a tetanus antitoxin titer generally relied upon to protect an individual against tetanus.

A purified and concentrated tetanus toxoid (tetanus toxoid topagen) for topical application intranasally was supplied to us by the Mulford Biological Laboratories of Sharp and Dohme.\* We have overcome Ramon's objection by the manner in which tetanus toxoid topagen is prepared and used as outlined in this report.

\*Tetanus toxoid topagen was prepared from highly antigenic plain tetanus toxoid. The toxoid was then purified and concentrated to contain 25 Lf's per c.c. Animal tests performed on guinea pigs that had been previously injected with alum toxoid, showed that tetanus toxoid topagen administered intranasally served as an excellent secondary stimulus.

We have used tetanus toxoid topagen intranasally on 145 human beings. The method of administration is simple. The patient is placed on a table with the head in hyperextension. An ordinary glass dropper is then inserted in the nose, with the blunt end pointing toward the turbinates. About 0.10 c.c. (two or three drops) of the tetanus toxoid topagen is then squeezed out by pressure on the rubber bulb. The patient is asked to "snuff up" the drops, and the dropper is then removed and wiped with an alcohol sponge. This process of instillation is repeated in the other nares. The subject is kept in the recumbent position for two or three minutes and is told not to blow his nose for a few hours. As expected, this request was not complied with in every case. The intranasal instillations were repeated daily or weekly, two or three times, as indicated in the text.

No attempts were made to select any of the patients. Several received the tetanus toxoid topagen while suffering from acute coryza, when their noses were stuffy and filled with mucus. No irrigating solutions or vasoconstrictor drugs were used prior to the instillation. Many patients had deviated nasal septa which made the introduction of the dropper difficult, and in four individuals the obstruction was so marked that the drug had to be dropped in at the external opening of the nose.

About one-third of the treated subjects complained of burning in the nose immediately after instillation of the drops. This lasted two or three minutes. In some, there was lacrimation. Two non-allergic patients sneezed frequently for a few hours following treatment. In subjects suffering from hay fever or allergic coryza there was a definite increase in the severity of this local reaction which assumed the form of a "head cold" that cleared up overnight. There was no disability. A few subjects complained of an unpleasant taste when the tetanus toxoid topagen reached the throat but this sensation disappeared rather quickly. The local reaction which was undoubtedly partly due to the high

glycerin content of the preparation did not interfere with completion of the course of instillations. No systemic reaction such as fever, malaise, urticaria or asthma was encountered. All patients preferred the nasal rather than the injection method of treatment.

*Clinical Results.* The 145 subjects undergoing treatment with tetanus toxoid topagen were divided into eight groups. Group A received tetanus toxoid topagen exclusively for the primary course of treatment. Groups B, C and D received one subcutaneous injection of alum precipitated tetanus toxoid and a series of intranasal instillations of tetanus toxoid topagen. Prior to nasal treatment Groups E, F, G and H were injected with two or more doses of alum precipitated toxoid or three or more doses of plain toxoid or toxoid (plain) with 0.4 per cent alum.

A control bleeding was obtained in each case just before the first tetanus toxoid topagen instillation. Thereafter, bleedings were taken at frequent intervals. The antitoxin titer of each sample of human blood serum was determined on guinea pigs in accordance with the standard technique of the National Institute of Health. As in previous communications we have in this report used 0.10 unit of antitoxin as the amount required to protect against clinical tetanus. This was arrived at from our studies on passive immunization against tetanus.<sup>28</sup> We realize that this base level of 0.10 unit may be too high, that is to say, less than 0.10 unit of tetanus antitoxin per c.c. of blood serum may be sufficient to protect man against infection with *Cl. tetani*. Yet until this question is definitely settled, we feel that it is safer to err on the side of conservatism.

Thirteen patients (Group A, Table 1) received two courses of tetanus toxoid topagen instillations. The first course consisted of three daily intranasal treatments (about 0.10 c.c. in each nostril). Ninety-two days later, eight patients received a second course of three daily instillations while five got two intranasal

treatments on successive days. In one instance the second course of treatment was given 106 days after the first, and it consisted of two nasal instillations given forty-eight hours apart.

The first course of intranasal instillations in Group A did not produce an appreciable increase in the antitoxin titer. Repeated titrations after completion of the second course of instillations showed less than 0.10 unit of antitoxin in all but three subjects. Case 222 showed more than 0.10 and less than 0.25 unit on the forty-seventh day, while Cases 223 and 303 had more than 0.10 and less than 0.25 unit and 0.25 unit respectively, on the fourteenth day. These last two patients displayed the same titer when retested on the forty-seventh and thirty-fourth days respectively.

Thirty-eight subjects (Groups B and C) were injected subcutaneously with the usual preparatory dose of 1.0 c.c. of tetanus toxoid alum precipitated. Ninety-one days later these individuals were treated intranasally with tetanus toxoid topagen (about 0.10 c.c. in each nostril). Twenty of them (Group B, Table II) received two daily treatments, while eighteen (Group C, Table III) received three such daily instillations.

In agreement with past findings, already reported,<sup>6,28-31</sup> the injection of the first dose of tetanus alum precipitated toxoid in these two groups failed to increase the titer to any appreciable extent. Seven days after intranasal treatment was instituted seventeen out of the twenty cases of Group B (Table II) showed less than 0.10 unit. The exceptions (421, 440, and 441) showed a definite increase in titer equal to or exceeding 0.10 unit. On the fourteenth day, all but one case showed 0.10 unit or more of tetanus antitoxin per c.c. of blood serum. The cases that responded to intranasal instillations of toxoid topagen showed antitoxin titers ranging from 0.10 unit to more than 1.0 and less than 3.0 units. The exception (430), when retested on the twenty-fifth day, showed more than 0.10 and less than 0.25 unit. The entire group

was retested thirty-four days after nasal treatment was started. Nine cases showed no change, eight showed a decrease and three showed an increase over the previously recorded antitoxin titer. Actually, nineteen cases had 0.10 unit or more of antitoxin while one patient had less than 0.10 unit.

Thirteen out of eighteen patients in Group C (Table III) who received three daily instillations, showed less than 0.10 unit when tested seven days after the first nasal treatment. The other five cases showed an increase in titer that assured good protection against tetanus. On the fourteenth day, sixteen out of the seventeen cases that were tested, showed a titer of 0.10 unit or more of tetanus antitoxin per c.c. of serum. The highest value was recorded in Case 413 with more than 8.0 units. The exception, Case 437, had less than 0.10 unit, but when retested eleven days later he showed more than 0.10 unit and less than 0.25 unit. On the thirty-fourth day, seven members of the group showed a decrease, six showed no change and two showed an increase in titer over the previously recorded antitoxin values. At this time all but two patients had more than 0.10 unit.

Group D (Table IV) included seven individuals treated the same as Group C, except that the interval between the injection of toxoid and the course of nasal instillations was 119 to 155 days. Follow-up titrations revealed that seven days after the first instillation, four subjects had more than 0.10 unit of antitoxin while three still showed less than 0.10 unit. On the fourteenth day, two of the three subjects that were tested evinced a further increase in their antitoxin titer. Case 203 showed the poorest response with 0.10 unit on the twenty-first day, dropping to more than 0.02 and less than 0.10 unit of antitoxin when tested on the ninety-first day. Similarly, Case 206 showed a drop from 0.50 unit on the thirty-first day, to less than 0.10 unit on the ninety-fourth day, and Case 201 had less than 0.10 unit when

retested 182 days after the first instillation of tetanus toxoid topagen.

Two members of Group D (Table v) were given a "repeat" dose intranasally after the antitoxin content of the blood had

nostril) 133 days after the first instillation. When tested two weeks later, both subjects showed more than 1.0 and less than 3.0 units. Their titers were well maintained upon retesting four to six weeks later.

TABLE I

## GROUP A

First course of treatment: Three daily intranasal instillations of tetanus toxoid topagen #544A, 0.1 c.c. in each nostril. Second course of treatment: Two or three daily intranasal instillations of tetanus toxoid topagen #544A, 0.1 c.c. in each nostril. Interval between the two courses of treatment, 92 days. Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Case	Control Titer	Days after First Nasal Treatment (1st Course)		Number of Intranasal Installations (2nd Course)	Days after First Nasal Treatment (2nd Course)				
		Titer	Titer*		Titer				
		30 Days	92 Days		7 Days	9 Days	14 Days	34 Days	47 Days
220	-0.01	-0.01	0.01 -0.02	Three	-0.02	-0.10	-0.10		
222	-0.01	-0.01	+0.01 -0.02	Three	-0.02	-0.10	-0.10	.....	+0.10 -0.25
223	-0.01	-0.01	+0.01 -0.02	Three	-0.02	-0.10	+0.10 -0.25	.....	+0.10 -0.25
301	-0.01	-0.01	-0.10	Three	-0.10	.....	-0.10	-0.10	
304	-0.01	-0.01	-0.10	Three	-0.10	.....	-0.10	-0.10	
305	-0.01	-0.01	-0.10	Three	-0.10	.....	-0.10	-0.10	
308	-0.01	-0.01	-0.10	Three	-0.10	.....	-0.10	-0.10	
310	-0.01	-0.01	-0.10	Three	-0.10	.....	-0.10		
221	-0.01	-0.01	-0.01†	Two‡	-0.10	.....	.....	-0.10	
302	-0.01	-0.01	-0.10	Two	-0.10	.....	-0.10	-0.10	
303	-0.01	-0.01	-0.10	Two	-0.10	.....	0.25	0.25	
307	-0.01	-0.01	-0.10	Two	-0.10	.....	-0.10	-0.10	
309	-0.01	-0.01	-0.10	Two	-0.10	.....	-0.10	-0.10	

\* Bleeding taken prior to first nasal instillation of second course of treatment.

† Bleeding taken 106 days.

‡ Second course of treatment consisted of two nasal instillations given 48 hours apart.

dropped to less than 0.10 unit. Case 203 got one such nasal instillation 161 days after the first tetanus toxoid topagen was administered, while Case 206 received two daily nasal treatments (0.10 c.c. in each

Group E consisted of twenty-eight individuals who received tetanus toxoid topagen intranasally on two successive days, as a "repeat" dose. (Table VI.) Prior to the intranasal administration of this

"repeat" dose, thirteen members of this group had been immunized with two injections of tetanus toxoid alum precipitated refined #26542-1, injected subcutaneously. Second course of treatment: Two daily intranasal instillations of tetanus toxoid topogen #544A, 0.1 c.c. in each nostril. Interval between the two courses of treatment, 91 days. Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

TABLE II

GROUP B

First course of treatment: 1.0 c.c. of tetanus toxoid alum precipitated refined #26542-1, injected subcutaneously. Second course of treatment: Two daily intranasal instillations of tetanus toxoid topogen #544A, 0.1 c.c. in each nostril. Interval between the two courses of treatment, 91 days. Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Case	Control Titer	Days after Injection of Toxoid		Days after First Nasal Treatment			
		Titer	Titer*	Titer			
				7 Days	14 Days	25 Days	34 Days
400	-0 01	-0 01	-0 10	-0 10	0 10		0 10
402	-0 01	-0 01	-0 10	-0 10	0 25		0 25
403	-0 01		-0 10	-0 10	+0 50 -1 0		+0 25 -0 50
406	-0 01		-0 10	-0 10	+1 0		+1 0
407	-0 01	-0 01	-0 10	-0 10	0 75		+0 50 -0 75
409	-0 01		-0 10	-0 10	0 10		0 10
421	-0 01		-0 10	0 25	1 0		+0 50 -1 0
423	-0 01		-0 10	-0 10	0 10		0 10
424	-0 01	-0 01	-0 10	-0 10	1 5		2 0
426	-0 01	-0 01	-0 10	-0 10	0 50		0 75
428	-0 01	-0 01	-0 10	-0 10	1 5		1 0
429	-0 01	-0 01	-0 10	-0 10	1 5		1 5
430	-0 01	-0 01	-0 10	-0 10	-0 10	+0 10 -0 25	-0 10
432	-0 01	-0 01	-0 10	-0 10	0 10		0 10
435	-0 01	-0 01	-0 10	-0 10	0 10		0 25
438	-0 01		-0 10	-0 10	0 75		+0 50 -1 0
440	-0 01	-0 01	-0 10	+0 25 -0 50	1 5		+0 50 -0 75
441	-0 01	-0 01	-0 10	0 10	+1 0 -3 0		+1 0 -3 0
442	-0 01	-0 01	-0 10	-0 10	0 50		0 50
443	-0 01	-0 01	-0 10	-0 10	0 50	+0 25 -0 50	0 25

\* Bleeding obtained prior to first nasal instillation

tions of tetanus toxoid alum precipitated; eight had gotten three such injections; one subject had received two doses of alum toxoid and a third injection of plain toxoid;

one patient had received five injections of alum toxoid; one had been injected with

TABLE III

GROUP C

First course of treatment: 1.0 c.c. of tetanus toxoid alum precipitated refined #26542-1, injected subcutaneously. Second course of treatment: Three daily intranasal instillations of tetanus toxoid topogen #544A, 0.1 c.c. in each nostril. Interval between the two courses of treatment, 91 days. Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Case	Control Titer	Days after Injection of Toxoid		Days after First Nasal Treatment			
		Titer	Titer*	Titer			
				7 Days	14 Days	25 Days	34 Days
401	-0 01	-0 01	-0 10	-0 10	0 25		+0 10 -0 25
404	-0 01	-0 01	-0 10	0 50	+5 0 -7 5		+1 0 -3 0
405	-0 01		-0 10	-0 10	0 10		-0 10
408	-0 01	-0 01	-0 10	-0 10	1 5		
410	-0 01		-0 10	-0 10	0 10		+0 10 -0 25
411	-0 01		-0 10	0 50	1 0		+0 50 -1 0
413	-0 01		-0 10	+1 0 -3 0	+8 0		+9 0 -10.0
414	-0 01	-0 01	-0 10	-0 10	1 0		+0 25 -0 50
415	-0 01		-0 10	-0 10	1 0		+1 0 -3 0
416	-0 01		-0 10	+0 10 -0 25	+1 0 -3 0		+1 0 -3 0
417	-0 01	-0 01	-0 10	-0 10			+0 10 -0 25
419	-0 01	-0 01	-0 10	-0 10	0 50		+0 25 -0 50
420	-0 01	-0 01	-0 10	-0 10	1 0		1 0
427	-0 01	-0 01	-0 10	0 10	1 5		1 5
431	-0 01	-0 01	-0 10	-0 10	1 0		1 0
434	-0 01	-0 01	-0 10	-0 10	0 5	.. .	0 5
437	-0 01		-0 10	-0 10	-0 10	+0 10 -0 25	-0 10
439	-0 01	-0 01	-0 10	-0.10	+0 10 -0 25		+0 10 -0 25

\* Bleeding obtained prior to first nasal instillation.

three doses of tetanus toxoid plus 0.4 per cent alum; two patients received four such doses, while two members had been



injected with four doses of plain tetanus toxoid. The time interval that elapsed between the last injection of toxoid and the first intranasal application of tetanus toxoid topagen is indicated in Table VI. Eight subjects had a control titer of less than 0.10 unit per c.c. of blood serum while the rest had 0.10 unit or more.

0.10 unit or more per c.c. of blood serum. Case 9951 actually had 5.0 units. Six patients showed the same antitoxin content as before intranasal stimulation. Two additional cases showed less than 0.10 unit but one of them, when tested for lower values showed some increase, though not sufficient to reach the 0.10 unit level. Of fourteen

TABLE IV

## GROUP D

First course of treatment 1.0 c.c. of tetanus toxoid alum precipitated refined, injected subcutaneously. Second course of treatment. Three daily intranasal instillations of tetanus toxoid topagen #544A, 0.1 c.c. in each nostril. Interval between the two courses of treatment, 119-155 days. Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Case	Days after Toxoid Injection	Days after First Nasal Treatment							
	Titer*	Titer							
200	119 days -0 10		7 days +0 10 -0 25						
201	119 days -0 10		7 days +0 10 -0 25			35 days 0 50		105 days +0 10 -0 25	182 days -0 10
202	119 days -0 10		7 days +1 0 -3 0	14 days +1 0 -3 0		32 days 3 0		91 days +1 0 -3 0	182 days 1 0
203	119 days -0 10	5 days -0 10	7 days -0 02		21 days 0 10	35 days +0 10 -0 25	49 days +0 10 -0 25	91 days +0 02 -0 10	161 days +0 01 -0 10
204	119 days -0 10		7 days +0 25 -0 50	14 days +1 0 -3 0		32 days 0 50		91 days +0 10 -0 25	192 days 0 10
206	155 days -0 02		7 days 0 02	17 days +0 50 -1 0		31 days 0 50		94 days -0 10	133 days -0 10
207	154 days -0 02		7 days 0 05		28 days +0 25 -0 50		.	98 days +0 10 -0 25	

\* Bleeding obtained prior to first nasal instillation.

Five days after the first tetanus toxoid topagen instillation, one out of ten tested showed an increase in titer from less than 0.10 to 0.10 unit. The rest had the same values as in the control tests. On the seventh day after the first instillation eighteen out of twenty-six showed a definite increase in titer. Those who had a control value of less than 0.10 unit showed

patients retested two days later, two showed no change in titer, while the rest displayed a marked increase. On the fourteenth day following the first instillation, the entire group with the exception of one patient, and four not tested, showed a further increase in titer, ranging from more than 0.25 to less than 12.0 units, an increase of from 2.5 to over 100 times the

control antitoxin values. The exception, case 9962, showed no increase over the titer obtained on the ninth day (0.25 unit).

When retested four to six weeks after intranasal stimulation was started, eight individuals showed no change from the previously recorded titer, eight showed an increase, while seven displayed a decrease. All patients had good antitoxic immunity. The values ranged from more

TABLE V  
GROUP D

First course of treatment: 1.0 c.c. of tetanus toxoid alum precipitated refined, injected subcutaneously. Second course of treatment: Three daily intranasal instillations of tetanus toxoid topagen #544A, 0.1 c.c. in each nostril. Third course of treatment: "Repeat stimulus" tetanus toxoid topagen #544A, 0.1 c.c. in each nostril. Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Case	Days between 1st and 2nd Course of Intranasal Instillation	Number of Intranasal Instillations, 2nd Course ("Repeat Stimulus")	Control Titer*	Days after First Nasal Treatment (Second Course "Repeat Stimulus")	
				Titer	
203	161	One	+0.01 -0.10	14 days +1.0 -3.0	42 days +0.50 -1.0
206	133	Two (successive days)	-0.10	13 days +1.0 -3.0	31 days 1.0

\* Bleeding obtained prior to first nasal instillation of second course ("repeat stimulus").

than 0.25 unit to 10 units per c.c. of blood serum.

Of twenty-five patients retested ninety-one to ninety-five days after nasal stimulation was initiated, seventeen showed a decrease, six showed the same and only two showed an increase over the previously recorded titer. In a few patients the loss in titer was marked, but in all cases the antitoxin values were still greater than those found before immunization, indicating good protection. Case 8096 had less than 0.10 unit when tested 114 days after the first topagen application. Case 7966 showed 0.10 unit when tested on the 144th day. Cases 210, 9915 and 9919 still showed good protection when tested six months after nasal stimulation.

As a "repeat stimulus" tetanus toxoid was given intranasally on three successive days to a group of twenty-nine subjects. (Group F, Table VII.) Prior to this nasal stimulation, twelve of these patients had been immunized with two injections of tetanus toxoid alum precipitated; ten had received three such injections; one had received four doses of alum precipitated tetanus toxoid; two had been injected with three doses of tetanus toxoid plus 0.4 per cent alum; two had three injections of plain tetanus toxoid while the remaining two members of group G had received four doses of plain toxoid. The interval of time that elapsed between the last injection of toxoid and the first intranasal application of tetanus toxoid topagen is indicated in Table VII.

Sixteen cases had a control titer of less than 0.10 unit per c.c. blood serum, while the rest had 0.10 unit or more of antitoxin. Five days after the first instillation seven patients were tested and only one showed an increase from less than 0.10 to 0.10 unit. On the following day (sixth day) two cases showed an increase in titer to and above 0.10 unit, while two others showed no change over the control values. The latter, however, showed an increase in titer when retested three days later. On the seventh day, twenty out of twenty-four cases that were tested showed a definite increase in titer to or above the 0.10 unit or control titer. Of the remaining four, three showed no increase above the control values. However, when retested two days later, the latter showed a marked increase in titer. The fourth case showed an increase of low magnitude, from 0.02 to 0.05 unit. When retested on the fourteenth day, this patient had 0.25 unit. Twenty-two patients were tested on the ninth day, and they each had an excellent antitoxin response. A further increase in titer was found on the fourteenth day; most patients had more than 1.0 unit. At the end of a month, the antitoxin titer was the same in thirteen cases, was increased in eleven and was reduced in four patients. Retests done on

TABLE VI

## GROUP E

Two daily intranasal instillations of tetanus toxoid topagen #544A, 0.1 c.c. in each nostril, given as a "repeat dose." Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Patient	Interval between Last Toxoid Injection and First Nasal Instillation, Days	Titer before Nasal Instillation	Days after First Nasal Instillation								
			Titer								
			5 Days	7 Days	9 Days	14 Days	30-31 Days	91-95 Days	128 Days	144 Days	182-196 Days
101**	657	-0.10	-0.10	0.10	.....	+ 0.25 - 0.50	+ 0.50 - 1.0	0.50			
103**	657	-0.10	-0.10	+0.25 -0.50	.....	+ 1.0 - 3.0	+ 1.0 - 3.0	+2.0 -3.0			
139**	657	-0.10	-0.10	0.50	.....	+ 8.0 -10.0	8.0	5.0			
9951**	902	-0.10	0.10	5.0	.....	+10.0 -12.0	10.0	7.0			
102**	657	-0.10	-0.10	-0.10	.....	+ 0.25 - 0.50	0.50	+0.25 -0.50			
124**	657	+0.02 -0.05	-0.10	+0.05 -0.10	.....	+ 0.50 - 1.0	+ 1.0 - 3.0	+0.50 -1.0			
119**	657	0.10	0.10	+0.10 -0.25	.....	+ 1.0 - 3.0	+ 3.0 - 5.0	+3.0 -5.0			
210**	949	+0.10 -0.25	+0.10 -0.25	.....	.....	+ 0.50 - 1.0	32 days 5.0	+1.0 -2.0	.....	....	+0.50 -1.0
123**	678	0.10	.....	+0.25 -0.50	3.0	+ 7.5 -10.0	7.0	+1.0 -3.0			
132**	678	+0.10 -0.25	.....	0.50	+1.0 -3.0	3.0	+ 1.5 - 2.0	+1.0 -2.0			
110**	678	0.25	.....	+0.25 -0.50	1.0	+ 1.5 - 3.0	+ 1.5 - 3.0	3.0			
9926**	923	+0.10 -0.25	.....	+0.25 -0.50	+1.0 -3.0	3.0	+ 1.0 - 3.0	+1.0 -3.0			
10013**	801	0.10	.....	+0.10 -0.25	0.50	+ 0.50 - 1.0	+ 0.75 - 1.0	1.0			
7966***	994	-0.10	.....	0.50	.....	.....	28 days + 1.0 - 3.0	0.25	.....	0.10	
8096***	592	-0.10	.....	0.10	10 days +0.10 -0.25	.....	38 days 0.25	114 days +0.05 -0.10			
9915***	525	0.10	0.10	+0.10 -0.25	.....	.....	35 days 0.50	0.25	.....	....	+0.10 -0.25
9906***	546	+0.50 -1.0	.....	.....	.....	5.0	42 days 5.0	3.0			
9919***†	475	+1.0 -3.0	+1.0 -3.0	+1.0 -3.0	.....	.....	42 days + 3.0 - 5.0	3.0	.....	....	3.0
500*****	559	0.10	.....	+0.10 -0.25	.....	+ 1.0 - 3.0	35 days + 1.0				
9943***	651	0.25	.....	+0.25 -0.50	3.0	+ 7.0 -10.0	6.0	+0.50 -1.0			
9955***	651	0.10	.....	+0.10 -0.25	+0.50 -0.75	+ 2.0 - 3.0	+ 2.0 - 3.0	+2.0 -3.0			
9953***	651	+0.10 -0.25	.....	+0.25 -0.50	+1.0 -3.0	3.0	+ 1.0 - 3.0	.....	+0.50 -1.0		
9931***	564	+0.25 -0.50	.....	+0.25 -0.50	+0.25 -0.50	+ 0.50 - 1.0	+ 0.50 - 1.0	+0.50 -0.75			
9978††††	564	+0.10 -0.25	.....	+0.10 -0.25	+0.10 -0.25	+ 0.25 - 0.50	0.50	0.25			
9983††††	564	+0.25 -0.50	.....	+0.25 -0.50	+0.50 -1.0	+ 0.75 - 1.0	1.0	+0.50 -1.0			
9976†††	934	0.50	.....	+0.50 -1.0	1.0	+ 1.5 - 3.0	+ 1.0 - 2.0	+0.50 -1.0			
9962††††	564	+0.10 -0.25	.....	+0.10 -0.25	0.25	0.25	+ 0.25 - 0.50	+0.10 -0.25			
9963††††	564	0.50	.....	0.50	+0.50 -0.75	+ 1.0 - 3.0	+ 1.0 - 3.0	+0.50 -1.0			

\* One injection of tetanus toxoid, alum precipitated received prior to nasal instillation.

† One injection of tetanus toxoid, plus 0.4 per cent alum received prior to nasal instillation

‡ One injection of tetanus toxoid, plain received prior to nasal instillation.

TABLE VII

## GROUP F

Three daily intranasal instillations of tetanus toxoid topagen #544A, 0.1 c.c. in each nostril, given as a "repeat dose." Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Patient	Interval between Last Toxoid Injection and First Nasal Instillation, Days	Titer before Nasal Instillation	Days after First Nasal Instillation								
			Titer								
			5 Days	6 Days	7 Days	9 Days	14 Days	30-34 Days	90-94 Days	128 Days	184-189 Days
100**	657	-0.10	-0.10	.....	0.25	.....	+1.0 -3.0	+1.0 -3.0	2.0		
112**	657	-0.10	-0.10	.....	+0.25 -0.50	.....	+1.0 -3.0	+1.0 -3.0	2.0		
121**	657	-0.10	-0.10	.....	+0.10 -0.25	.....	+1.0 -3.0	+1.0 -3.0	+0.50 -1.0		
136**	657	-0.10	-0.10	.....	0.10	.....	1.0	1.0	+0.50 -1.0		
131**	609	-0.10	.....	0.10	.....	+0.50 -1.0	.....	+1.0 -3.0	+1.0 -3.0	.....	+3.0 -4.0
134**	609	-0.10	.....	+0.10 -0.25	.....	+1.0 -3.0	.....	+3.0 -5.0	+0.50 -1.0	.....	+0.25 -0.50
9949**	854	-0.10	.....	.....	0.50	+1.0 -3.0	.....	+5.0 -10.0	5.0	.....	+1.0 -3.0
10007**	732	-0.10	.....	-0.10	.....	+0.25 -0.50	.....	0.50	0.50	.....	0.50
104**	657	0.02	-0.10	.....	0.05	.....	0.25	+0.25 -0.50	+0.25 -0.50		
125**	609	0.10	.....	0.10	.....	+0.10 -0.25	.....	+0.25 -0.50	+0.25 -0.50	.....	+0.10 -0.25
115**	678	0.50	.....	.....	+0.50 -1.0	+0.75 -1.0	+1.0 -3.0	+1.0 -3.0	.....	+0.50 -1.0	
117**	678	0.25	.....	.....	0.50	+1.0 -3.0	+5.0 -7.5	5.0	+1.0 -3.0		
9946***	630	-0.10	0.10	.....	+0.10 -0.25	.....	+0.50 -1.0	1.0	0.50		
10002***	582	-0.10	.....	.....	+0.10 -0.25	0.25	.....	0.25	+0.10 -0.25	.....	0.10
9944***	582	-0.10	.....	.....	.....	1.0	.....	+1.0 -3.0	+1.0 -3.0	.....	+0.50 -1.0
9939***	651	0.10	.....	.....	0.25	+0.50 -1.0	+1.0 -3.0	+1.0 -3.0	+0.50 -1.0		
9948***	651	+0.25 -0.50	.....	.....	+0.50 -1.0	+1.0 -3.0	+1.5 -3.0	2.0	+1.0 -2.0		
9933***	651	0.25	.....	.....	+1.0 -3.0	6.0	6.0	+3.0 -5.0	+1.0 -3.0		
9928***	564	+0.25 -0.50	.....	.....	+1.0 -3.0	5.0	5.0	+3.0 -5.0	+1.0 -3.0		
10012***	564	0.25	.....	.....	+0.25 -0.50	1.0	6.0	+3.0 -5.0	1.0		
9942***	651	+0.25 -0.50	.....	.....	+0.25 -0.50	0.50	+1.0 -3.0	+1.5 -3.0	+1.0 -2.0		
9941***	651	0.25	.....	.....	0.25	1.0	+1.5 -3.0	+2.0 -3.0	+1.0 -2.5		
7756****	959	-0.10	-0.10	.....	+0.25 -1.0	.....	+3.0 -5.0	+3.0 -5.0	3.0	.....	+1.0 -3.0
9982†††	948	-0.10	.....	.....	0.10	+0.50 -1.0	+1.0 -3.0	+1.0 -3.0	1.0		
9973†††	878	-0.10	.....	.....	+0.25 -0.50	1.0	.....	+3.0 -5.0	3.0	.....	1.5
9964†††	865	-0.10	.....	.....	+0.50 -1.0	+1.0 -3.0	.....	+5.0 -10.0	5.0	.....	+0.50 -1.0
9970†††	879	0.25	.....	.....	+0.50 -1.0	0.50	.....	+1.0 -3.0	+1.0 -3.0	.....	1.0
9986†††	564	+0.10 -0.25	.....	.....	0.25	0.50	+0.25 -0.50	+0.25 -0.50	0.25		
9968†††	564	+0.25 -0.50	.....	.....	+0.25 -0.50	+0.50 -1.0	+1.0 -3.0	+1.0 -3.0	+0.50 -1.0		

\* One injection of tetanus toxoid, alum precipitated received prior to nasal instillation.

† One injection of tetanus toxoid, plus 0.4 per cent alum received prior to nasal instillation.

‡ One injection of tetanus toxoid, plain received prior to nasal instillation.

twenty-eight patients ninety to ninety-four days after the initial nasal instillation, showed a decrease in titer in eighteen cases. Notwithstanding this loss in antitoxin, their titers were still far above the control values, assuring protection against tetanus. Case 115 showed more than 0.50 and less than 1.0 unit when tested 128 days after nasal stimulation. Eleven were retested six months after the first instillation of tetanus toxoid topagen and they all had more than 0.10 unit. Five of these patients actually had 1.0 unit or more of antitoxin per c.c. of blood serum.

Group G (Table VIII) consisted of twenty-one individuals who received two intranasal applications of tetanus toxoid topagen, a week apart. Prior to this stimulation, eleven patients had been immunized with two injections of alum precipitated tetanus toxoid; seven had received three such injections; one had three doses of tetanus toxoid plus 0.4 per cent alum, and two patients had received four doses of the latter antigen. The time interval that elapsed between the last injection of toxoid and the first intranasal instillation is indicated in Table VIII.

Before application of the tetanus toxoid topagen nine patients had less than 0.10 unit of tetanus antitoxin per c.c. of blood serum. The other twelve had 0.10 unit or more. Five days after the first intranasal instillation, two showed an increase in titer from less than 0.10 to 0.10 unit while six had less than 0.10 unit. The entire group was bled seven days after a single nasal application, just before the second instillation. The sera of ten showed a definite increase in titer above the control values, more than sufficient to afford protection. Two additional patients showed an increase from a control titer of 0.05 unit to more than 0.05, but less than 0.10 unit. Nine subjects showed no change in titer. In three of these the titer remained less than 0.10 unit.

Two days after the second nasal instillation of tetanus toxoid topagen, eleven out of thirteen subjects tested showed a further

definite increase in titer, ranging from 0.10 to 12.5 units per c.c. of blood serum., while two showed the same titers as in the control test. However, when retested on the seventh day after the second intranasal application (fourteenth day after the initial application), these two patients showed a decided jump in antitoxin titer, and the entire group displayed an increase ranging from more than 0.25 to more than 20.0 units.

This remarkable antitoxin response was maintained in six subjects, was further increased in ten and was somewhat decreased in five members of the group at a retest a month after the first tetanus toxoid topagen instillation. The highest value we have ever encountered since we began active immunization of human beings against tetanus, was shown by Case 9937 with 30.0 units of antitoxin per c.c. of blood serum. A loss in titer was noted in all but three cases when the group was retested ninety-three to ninety-four days after intranasal stimulation. Yet notwithstanding this decrease in titer, the antitoxin values ranged from 0.25 to more than 15.0 and less than 20.0 units, an increase in several cases of sixty to 150 times over the control titer.

Group H (Table IX) consisted of nine patients who received three weekly intranasal instillations of tetanus toxoid topagen. Before nasal treatment was instituted, four had been injected with two doses of alum precipitated toxoid, one with three such doses, two with three doses of toxoid plus 0.4 per cent alum and two with three injections of plain toxoid. The interval that elapsed between the last toxoid injection and the first intranasal instillation is indicated in Table IX. Before treatment with tetanus toxoid topagen each patient had less than 0.10 unit of antitoxin per c.c. of blood serum. Seven days after the first and just before the second instillation five patients were bled and their sera titrated. Three showed an increase in titer to or above 0.10 unit, while the other two showed the same values as in the control tests.

TABLE VIII

## GROUP G

Two weekly intranasal instillations of Tetanus toxoid topagen #544A, 0.1 c.c. in each nostril, given as a "repeat dose." Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Patient	Interval between Last Toxoid Injection and First Nasal Instillation, Days	Titer before Nasal Instillation	Days after First Nasal Instillation					
			Titer					
			5 Days	7 Days	9 Days	14 Days	30-31 Days	93-94 Days
105**	657	-0.10	0.10	+0.25 -0.50	.....	+3.0 -5.0	+5.0 -10.0	+6.0 -7.5
107**	657	-0.10	0.10	+0.10 -0.25	.....	+1.0 -3.0	+3.0 -4.0	3.0
113**	657	-0.10	-0.10	+0.50 -3.0	.....	+3.0 -5.0	+3.0 -5.0	+3.0 -3.5
137**	657	-0.10	-0.10	0.10	.....	+5.0 -8.0	+5.0 -8.0	3.0
109**	657	0.05	-0.10	+0.05 -0.10	.....	+0.25 -0.50	0.50	+0.25 -0.50
116**	657	0.02	-0.10	0.02	.....	+1.0 -3.0	+5.0 -6.0	3.0
127**	657	-0.10	-0.10	-0.10	.....	+0.50 -1.0	1.0	0.75
120**	678	+0.25 -0.50	.....	+0.25 -0.50	1.0	+1.0 -3.0	2.0	+1.0 -2.0
126**	678	+0.10 -0.25	.....	+0.10 -0.25	0.25	+1.0 -3.0	+1.0 -3.0	+1.0 -1.5
10,006**	801	0.25	.....	+0.25 -0.50	+1.0 -3.0	15.0	11.0	+5.0 -7.5
9937**	923	0.25	.....	3.0	12.5	+20.0	30.0	+15.0 -20.0
9947***	630	-0.10	-0.10	-0.10	.....	+0.50 -1.0	1.0	0.50
9925***	651	+0.25 -0.50	.....	+0.50 -0.75	0.75	3.0	+1.0 -3.0	1.0
9954***	651	+0.50 -1.0	.....	1.0	+1.5 -3.0	2.0	+1.0 -2.0	+1.0 -2.0
9932***	564	0.25	.....	+0.50 -1.0	+1.0 -3.0	3.0	+1.0 -3.0	+0.50 -1.0
10,004***	564	+0.50 -0.75	.....	+0.50 -0.75	0.75	+1.0 -3.0	+1.0 -3.0	+1.0 -1.5
10,005***	564	0.10	.....	0.10	0.10	+0.25 -0.50	+0.25 -0.50	0.25
10,008***	564	0.10	.....	+0.10 -0.25	0.50	+3.0 -5.0	1.5	+0.25 -0.50
9979†††	934	+0.10 -0.25	.....	+0.10 -0.25	+0.10 -0.25	+0.50 -1.0	+1.0 -3.0	+1.0 -3.0
9975††††	564	0.05	.....	+0.05 -0.10	0.10	+0.50 -1.0	1.0	+0.50 -1.0
9985††††	564	0.10	.....	0.10	+0.10 -0.25	+0.25 -0.50	0.50	+0.25 -0.50

\* One injection of tetanus toxoid, alum precipitated received prior to nasal instillation.

† One injection of tetanus toxoid, plus 0.4 per cent alum received prior to nasal instillation.

Seven days after the second (fourteenth day after the first application) and just before the third instillation, the entire group was bled. Their sera showed an increase in titer that ranged from more than 0.25 to 8.0 units. A week after the third instillation five cases showed a further increase while four showed the same antitoxin values. All cases but one showed a decrease in titer ninety days after the initial intranasal stimulation. The titers of

ever, well above the control values, assuring protection against tetanus.

#### DISCUSSION

An analysis of the results obtained in our Groups A, B, and C (Table I, II and III) reveals the importance of the rôle played by the first subcutaneous injection of alum toxoid. Within the limits of dosage and schedule used by us it is apparent from the results obtained in our Group A that the subcutaneous dose cannot be uniformly replaced by three daily intranasal instillations of tetanus toxoid topagen. It would appear that in order to render the antitoxin-producing cells of the body capable of responding to subsequent stimulation by intranasally administered toxoid, it is necessary to introduce within the host a definite amount of toxoid. This did not take place in our Group A. We do not know whether this is due to differences in the amounts absorbed through the nasopharyngeal mucosa as compared to the quantity deposited under the skin, or whether a qualitative factor inherent to the different portals of entry of the toxoid is responsible for it. Experiments are now under way to rule out the first possibility. However, regardless of cause, we may conclude that all subjects must first receive a dose of alum toxoid subcutaneously in order that they may be able to react to subsequent stimulation through the mucous membrane of the nose.

A comparison of Tables II and III reveals the fact that a greater number of subjects reached the 0.10 unit level of antitoxin earlier in Group C, which received three daily instillations than in Group B which received two daily instillations, and that the magnitude of the antitoxin response was greater in Group C. On the other hand, at the end of thirty days, two members of Group C dropped below the 0.10 unit level, while only one patient in Group B showed at this time less than 0.10 unit. However, since a small number of individuals were involved, we must consider these findings as suggestive only.

TABLE IX  
GROUP H

Three weekly intranasal instillations of tetanus toxoid topagen #544A, 0.1 c.c. in each nostril, given as a "repeat dose." Titer expressed in units of tetanus antitoxin per c.c. of blood serum.

Patient	Interval between Last Toxoid Injection and First Nasal Instillation, Days	Titer before Nasal Instillation	Days after First Nasal Instillation				
			Titer				
			7 Days	14 Days	21 Days	90 Days	184 Days
122**	609	-0.10	.....	+1.0	+1.0 -3.0	+1.0 -3.0	+0.25 -0.50
130**	609	-0.10	.....	+3.0 -3.5	3.0	+0.50 -1.0	+0.25 -0.50
135**	609	-0.10	0.10	2.0	2.0	+0.50 -1.0	+0.25 -0.50
9936**	854	-0.10	+0.50 -1.0	8.0	8.0	+3.0 -5.0	+1.0 -3.0
9945***	582	+0.50 -0.10	+0.50 -0.10	+1.0 -3.0	+3.0 -5.0	1.0	+0.25 -0.50
9984†††	879	+0.05 -0.10	+0.05 -0.10	+0.25 -0.50	+0.50 -1.0	+0.50 -1.0	+0.50 -1.0
9981†††	879	-0.10	.....	+0.50 -1.0	+3.0 -5.0	0.50	+0.25 -0.50
9969†††	851	-0.10	.....	+0.25 -0.50	+0.50 -1.0	0.50	0.50
9960†††	865	-0.10	0.10	+2.0 -3.0	+5.0 -8.0	+1.0 -3.0	+0.50 -1.0

\* One injection of tetanus toxoid alum precipitated received prior to nasal instillation.

† One injection of tetanus toxoid plus 0.4 per cent alum received prior to nasal instillation.

‡ One injection of tetanus toxoid plain received prior to nasal instillation.

the group ranged from 0.50 to more than 3.0 and less than 5.0 units. Case 122 showed no change from the previous test. When retested 184 days after intranasal stimulation, all cases except two showed a further reduction in their titers which were, how-

It is interesting to compare the results obtained in Groups B, C and D (Table II, III and IV) with the titer that develops after the subcutaneous injection of a second dose of tetanus alum precipitated toxoid, as reported in previous communications.<sup>6,30,33</sup> In the latter, we find that out of twenty-four subjects that were tested seven days after the second injection of alum toxoid, six showed less than 0.10 unit, while the rest had 0.10 unit or more of antitoxin per c.c. of blood serum. On the fourteenth or fifteenth day, twenty-six subjects were tested and all had 0.10 unit or more of antitoxin, indicating good protection. Forty-five subjects that were tested one month after the second injection of toxoid showed more than 0.10 unit of antitoxin. (We have excluded one individual who was refractory to two injections of toxoid.) These differences are well illustrated in Chart 1. It would therefore appear that the antitoxin protection produced by intranasal tetanus toxoid topagen develops less promptly and is not so lasting as that which follows the injection of a second dose of tetanus alum precipitated toxoid.

Table V brings out the effective response obtained by the use of tetanus toxoid topagen intranasally as a "repeat" dose in two patients who had received the basic course of immunization by the combined subcutaneous and intranasal routes.

In the remaining groups of subjects reported in this paper (Tables VI, VII, VIII and IX) we are concerned with the value of tetanus toxoid topagen given intranasally in lieu of a "repeat" injection of tetanus toxoid alum precipitated. The eighty-seven subjects included had developed a substantial immunity as the result of the previous injection of two or more doses of tetanus toxoid.

A comparative study of our results indicates that at the end of one week after the first instillation of tetanus toxoid topagen, ten members of Group G (Table VIII) which, by this time, had received only one nasal application, showed an increase

in titer above that of the control test, while fourteen subjects showed no increase over the control values or still had less than 0.10 unit of antitoxin. Two additional subjects showed an increase over the control titer but not sufficient to reach the 0.10 unit level. On the other hand, in Group E (Table VI) which had received two nasal instillations on successive days, eighteen individuals showed an increase over the control titer, while seven showed the same values as in the control bleeding. One subject showed an increase, but not sufficient to reach 0.10 unit. In Group F (Table VII) which had received three nasal applications of tetanus toxoid topagen on successive days, twenty-two subjects showed an increase over the control values, while four showed either no increase or had less than 0.10 unit. These results hold true, even when these three groups of subjects are further subdivided in accordance with (1) the number of injections received prior to stimulation by tetanus toxoid topagen, or (2) whether the level of antitoxin prior to intranasal instillation was above or below 0.10 unit. In Groups E and F about the same number of individuals showed a further increase in titer between the seventh and ninth day after the first tetanus toxoid topagen instillation. In Group G, following the administration of the second intranasal dose, there was a definite increase in the number of individuals that showed a rise in titer two days later. At the end of two weeks, there was no great difference between the three groups, judging by the number of individuals that showed a rise in titer.

Analyzed from another angle, the findings show that on the ninth day after the first nasal instillation, two subjects in Groups E and G failed to show any increase over the control titer, while in Group F all subjects showed an increase. Naturally in Group G this may have been due to the short interval that elapsed between the second tetanus toxoid topagen instillation and the time of testing.



These findings would seem to indicate that three nasal instillations of tetanus toxoid topagen on successive days produce

Thus, in Case 10002 (Table VII), who showed the poorest response of all the individuals under study, the titer was

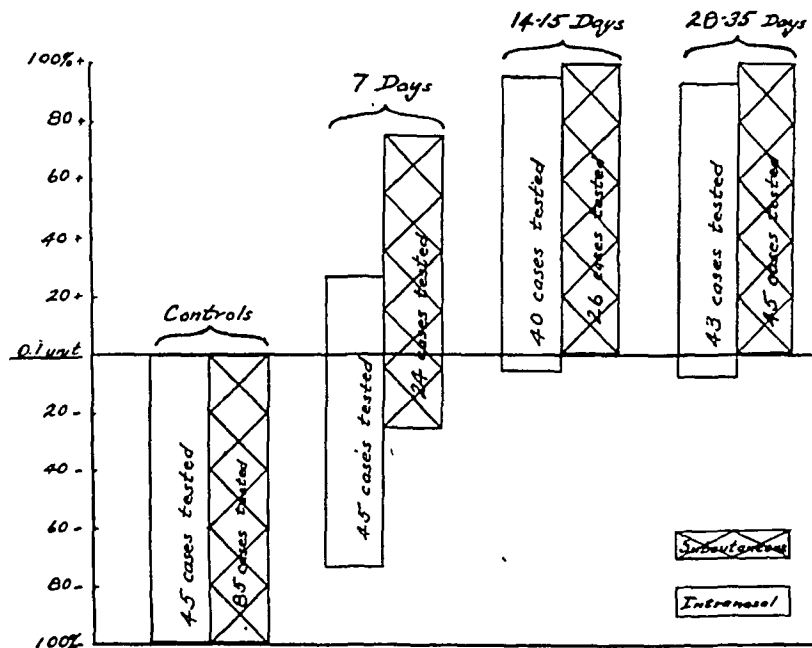


CHART 1. Comparison of the percentage of patients showing at least 0.10 unit of tetanus antitoxin following completion of the primary course of immunization in two groups of patients. One received two subcutaneous injections of alum precipitated toxoid while the other group received one subcutaneous injection of alum toxoid and a series of nasal instillations of tetanus toxoid topagen.

a more rapid rise in antitoxin titer than do two daily or two weekly instillations. Group H (Table IX), which received three weekly nasal applications of toxoid, did not show better immediate results than Group G. (Table VIII.)

Little can be said about differences in the level of antitoxin titer present in these groups. Individual variability in response is so marked that no comparisons can be made.

There did not appear to be any gross difference in the response elicited when the tetanus toxoid topagen was administered to subjects who had been previously immunized with two doses of toxoid as compared with those who had received from three to five toxoid injections. But regardless of the influence exerted by these factors, we do know that at the end of two to four weeks, all subjects were in possession of a large amount of tetanus antitoxin.

equivalent to that obtained after the subcutaneous injection of about 3000 units of tetanus antitoxin. In Case 9937 (Table VIII) who showed the highest titer, it was equivalent to the titer produced by the subcutaneous injection of about 450,000 units of tetanus antitoxin.

At the end of three months all the patients under consideration with the exception of Case 9962 (Table VI) had an antitoxin titer well above the control value, although in many it was not so high as at the end of thirty days. Twenty-three members of Groups E, F and H (Tables VI, VII and IX) showed good protection when tested six months after the "repeat" nasal stimulation.

A comparison of the antitoxin titer obtained after "repeat" stimulation by intranasal tetanus toxoid topagen with that produced by the subcutaneous injection of 1.0 c.c. of tetanus toxoid alum precipi-

tated in subjects that had received a basic course of immunization (two injections of alum toxoid, ninety days apart)<sup>32</sup> reveals

munity present at the time of stimulation. Differences in the time interval that separated the administration of the various

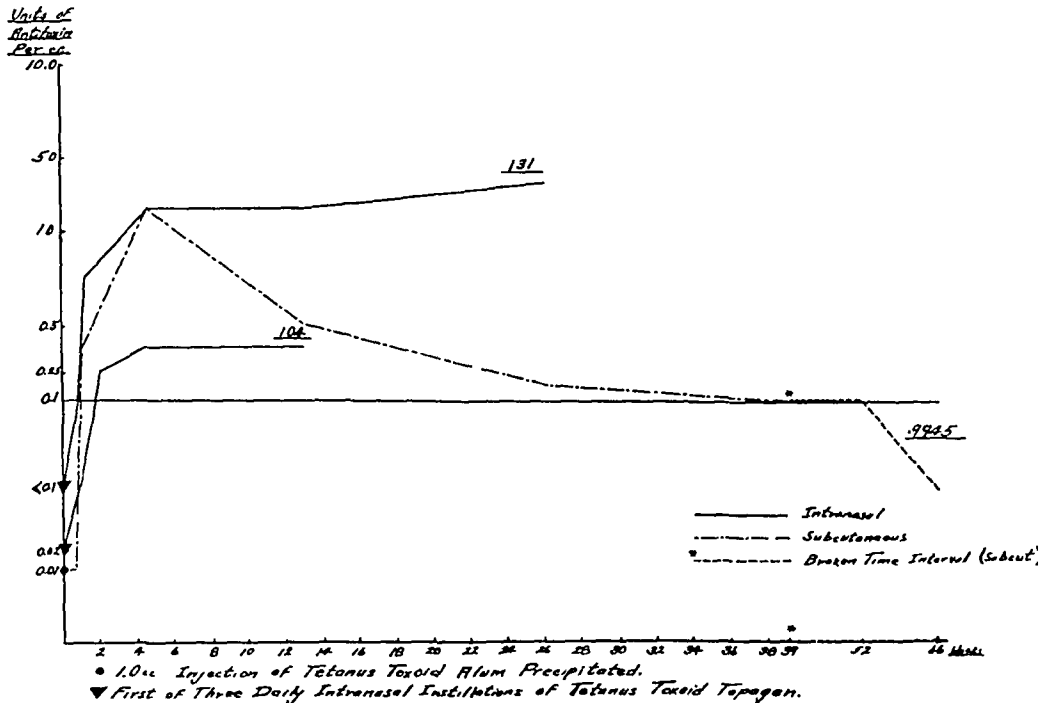


CHART II. Typical responses to tetanus toxoid topagen given intranasally as a "repeat dose." An average antitoxin curve obtained after the subcutaneous injection of alum toxoid as a "repeat dose" is plotted for comparative purposes.

the fact that in the latter the response is more prompt and the titer reaches a higher level earlier than when intranasal toxoid is used. Thus, after a "repeat" toxoid injection, the antitoxin titer reaches the 0.10 unit level in five to seven days, while after three daily nasal instillations given as a "repeat" dose it may take seven to nine days. Also the average titer at the end of a week after a repeat stimulus is administered is higher after a toxoid injection. However, after fourteen to thirty days, there is no gross difference in the height of antitoxic immunity present in the two groups. In some of the subjects that had received a third injection of toxoid prior to intranasal stimulation with tetanus toxoid topagen, the titer produced by the latter was not so high as that which followed the toxoid injection.<sup>30,31,32</sup> This may have been due not so much to the difference in the method of administration of the toxoid as to the state of antitoxic im-

stimulating doses of toxoid must also be considered. In some subjects, such as Case 8096, who was an allergic individual, the poorer response after intranasal toxoid was no doubt due to poor absorption through the nasal mucosa as a result of the local reaction that ensued. In this type of individual it may perhaps be worth while to increase the number of instillations. Typical responses to intranasal stimulation are illustrated in Chart II.

It is clear that when tetanus toxoid topagen is given intranasally to individuals who had been previously injected with one, two, or more subcutaneous doses of tetanus alum precipitated toxoid, it acts as a good secondary stimulus resulting in a remarkable elevation of the antitoxin titer. This rise appears to be sufficiently prompt and should prove valuable if the intranasal toxoid is routinely given in advance of injury.

At present, we recommend that a course of nasal instillations should consist of three daily treatments (0.1 c.c. of tetanus toxoid topagen in each nostril) repeated every six months. This schedule and dosage are not final. Future work may show that better results can be secured by giving two daily instillations, repeated a week later.

Present experience has convinced us that the combined subcutaneous and intranasal method of immunization against tetanus is practical. It can be carried out with ease in controlled populations, such as the army and navy, and also in large industrial plants, whose employees are subject to frequent injuries.

#### COMMENT

Active protection against tetanus, both acute and chronic, is highly desirable. While undoubtedly efficacious, immunization by means of tetanus toxoid administered parenterally, has the drawback of requiring repeated injections at the time of injury. Intranasal immunization against tetanus is feasible and practical if it is looked upon as a means of creating a state of antitoxic immunity in advance of an injury. In order to produce and maintain this state of immunity, it is necessary first to render the subject capable of responding to tetanus toxoid topagen stimulation intranasally by means of the previous injection of a primary course of two 1.0 c.c. doses of tetanus alum precipitated toxoid given ninety days apart, and second, to repeat the course of nasal instillations every six months.

#### CONCLUSIONS

1. Tetanus toxoid topagen when instilled in the nose is absorbed rapidly and in sufficient quantity to bring about a rise in antitoxin titer, in subjects who had previously undergone active immunization against tetanus by means of one or preferably two injections of tetanus alum precipitated toxoid.

2. When 0.10 c.c. of tetanus toxoid topagen is dropped into each nostril on two

or three successive days, or at weekly intervals, it will raise the antitoxin titer of actively immunized individuals from less than 0.10 unit to or above the 0.10 unit level in seven to nine days. The titer will remain above the protective level for at least several months.

3. No systemic reactions, and only a transient local nasal reaction, occur after instillations of tetanus toxoid topagen.

4. Active immunity can be maintained in advance of an injury by the repeated use of tetanus toxoid topagen intranasally. A course of three daily instillations should be repeated every six months.

I wish to thank the Mulford Biological Laboratories, Sharp and Dohme for the advice and coöperation given us throughout this experiment. I also wish to express my appreciation to Dr. E. A. Whitney, Medical Director of the Elwyn Training School, Elwyn, Pennsylvania, for allowing me to use inmates of this institution as subjects for this investigation. Allergic subjects included in this study were patients of the Allergy Clinic of the Chester Hospital.

#### REFERENCES

1. RAMON, G., and ZOELLER, C. *Compt. rend. Soc. de biol.*, 112: 347, 1933.
2. SACQUEPEE, E. *Paris méd.*, 1: 491, 1933.
3. SNEATH, P. A. T., and KERSLAKE, E. G. *Canad. M. A. J.*, 32: 132, 1935.
4. BERGEY, D. H. *J. Infect. Dis.*, 55: 72, 1934.
5. JONES, F. G., and MOSS, J. M. *J. Immunol.*, 30: 115, 1936.
6. GOLD, H. J. *A. M. A.*, 109: 481, 1937.
7. HALL, W. W. *Mil. Surgeon*, 80: 104, 1937.
8. MCBRYDE, A. *South. M. J.*, 30: 565, 1937.
9. COWLES, P. B. *Yale J. Biol. & Med.*, 9: 409, 1937.
10. BOYD, J. S. K. *J. Roy. Army M. Corps*, 70: 289, 1938.
11. SEWALL, H. *Science*, 62: 293, 1925.
12. SANARELLI, G. *Compt. rend. Soc. de biol.*, 91: 1302, 1924.
13. FRIEDMAN, E., ESSERMAN, A., and BLACK, M. H. *J. Pediat.*, 5: 504, 1934.
14. MAJOR, R. H. *J. Lab. & Clin. Med.*, 21: 278, 1935.
15. GEILING, E. M. K. *Glandular Physiology and Therapy*. Chicago, 1935. A. M. A.
16. SLESINGER, H. A. *J. Pediat.*, 9: 42, 1936.
17. GOLD, H. *J. Pediat.*, 10: 641, 1937.
18. DSERZGOWSKY, S. K. *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 2: 602, 1910.
19. ZOELLER, C., and RAMON, G. *Bull. Acad. de méd de Paris*, 97: 849, 1927.

20. ZOELLER, C., and RAMON, G. *Presse méd.*, 35: 1049, 1927.
21. RAMON, G., and ZOELLER, C. *Compt. rend. Soc. de biol.*, 97: 701, 1927.
22. RAMON, G., and ZOELLER, C. *Compt. rend. Soc. de biol.*, 96: 762, 1927.
23. LESNE, E., et al. *Compt. rend. Soc. de biol.*, 96: 1205, 1927.
24. SALVIOLO, G. *Pediatrics*, 36: 687, 1928.
25. JENSEN, C. *Proc. Roy. Soc. Med.*, 30: 1117, 1937.
26. BOUSFIELD, G., and KING-BROWN, W. W. *Lancet*, 1: 491, 1938.
27. WENGER, L. J., HAMPIL, B., and MASUCCI, P. *J. Bact.*, 36: 332, 1938.
28. GOLD, H. *J. Allergy*, 8: 230, 1937.
29. GOLD, H. *J. Lab. & Clin. Med.*, 23: 903, 1938.
30. GOLD, H. *J. Allergy*, 9: 545, 1938.
31. GOLD, H. *Ann. Int. Med.*, 13: 768, 1939.
32. GOLD, H. *J. Lab. & Clin. Med.*, 25: 506, 1939.
33. GOLD, H. Unpublished data.



THE modern pointed bullet is more unstable than the blunt-nosed Mauser type, and inflicts more severe damage on internal organs. That is to say, there are relatively fewer clean perforations of bone and viscera, and more damage is done to the internal organs in the way of laceration and disruption.

From—"War Wounds and Air Raid Casualties" (Lewis).

# THE CARE OF ADVANCED CANCER EXCLUSIVE OF THE RELIEF OF PAIN BY DRUGS\*†

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IT may not be generally appreciated that statistically we cure very few cancer patients. Perhaps we cure 15 to 20 per cent of breast cancers (10 per cent of the total incidence of cancer); 10 to 15 per cent of cervical cancers (12 per cent of the total); an occasional rectal and colon cancer (15 per cent of the total), practically no stomach cancer (33 per cent of the total). Therefore the great bulk of all carcinoma patients must be cared for through a more or less protracted terminal illness (three months to three years), when the outlook is hopeless and the physician and family are often times discouraged. But, nevertheless, the patient is a human being, entitled to whatever expert care we can give or suggest.

Wild,<sup>1</sup> after a twenty-six year service in the care of these patients, wrote: "There is no greater test of the capacity of a medical man than his ability to retain the confidence of a patient who is steadily going downhill, and the management of a case of inoperable cancer will tax all the tact, knowledge and skill of the ablest practitioner."

The first consideration is the psychological approach. Should one tell a patient he has hopeless cancer? It is often a difficult situation, which must be answered differently for different types of people and personalities.

Wild was strongly of the opinion that it is most desirable to hold out the hope of recovery even to the last. The mental

outlook of a man who believes his condition to be absolutely hopeless is quite different from that of a man who believes that he has even one chance in a thousand of recovery. It is usually best for the patient's morale not to tell him directly that he has a hopeless disease. "There is but one place where a man may wisely be thoughtless, his deathbed. No thinking should be done there," wrote Ruskin.<sup>2</sup> Hertzler feels that the average doctor is inclined to agree with him. From his crowded lifetime of intimate human contacts, Hertzler continues: "The most disastrous results may follow a tactless warning of even the true conditions. The family, or one member of it, may, as a matter of protection to the doctor, be given the true statement of the facts. One must use caution in the selection of the confidant, lest the information be blabbed to the patient, not through viciousness but just through the habit of telling all they know, plus imagination."

But there are exceptions, and each case must be handled individually. "Some patients tell the doctor they wish to know the truth, and by their bearing convince him that they mean it. I once had a patient of this type, a huge mountain of a man, a noted sheriff of the Southwest. For thirty years he had faced bandits and death many times in his career and he did not fear death from cancer. . . . Hope springs eternal. Some people refuse to recognize the fact when presented to them by the course of the disease. I once saw in

\* From Mercy Hall Tumor Clinic and Hospital, Detroit, Michigan. Presented as a scientific exhibit at the meeting of the American Medical Association in San Francisco, 1938.

† A second article, entitled: "A Régime for Controlling Pain in Far Advanced Cancer" will follow in a succeeding issue.

consultation a very intelligent woman in the advanced stages of cancer of the breast. As I looked at the huge ulcerating mass she mildly remarked: 'You think you see a tumor, but you are wrong. There is none there; I am going to get well!' She denied that she suffered pain. . . .

"Sometimes the situations take on other forms. I once had a fine old gentleman with a cancer of the stomach. I told him that all I could do was to relieve, in a measure, his pain. He only asked to die to relieve his wife and his daughter of the care of him throughout the months to which my prognosis condemned him. Though he would leave them moderately comfortable financially, yet he had not enough to bear the expense of prolonged care."

In our experience, not more than 15 to 20 per cent of cancer patients are depressed. The instances where we have told a patient he or she has hopeless cancer are not many. They have been chiefly the intelligent persons, usually of phlegmatic disposition, who we have felt might coöperate better if they know all—and this has invariably been after a certain amount of acquaintance with the patient.

What is important is that the patient have cheerful surroundings and attendants. "Much of the gloom which surrounds some patients emanates from attendants, and this must not be. The physician should see to it that tranquility and beauty are found in the patient's environment and that anything which unduly irritates him is avoided."<sup>3</sup>

Symptoms can be discussed frankly, with never an air of hopelessness. Direct questions about prognosis can almost always be evaded or parried.

*Nursing Care.* If these patients are grouped in a service for far advanced care, much can be done for them by specialized nursing. The nursing staff is allowed more initiative than in ordinary hospital ward care, carrying out all ward therapy, including dressings, under supervision. A hospital bed, frequent change of bed linen, bodily

warmth, cleanliness, may be sufficient to relieve pain.

Individual narcotic medication can also be handled better by the nurse in charge, under close supervision, than if the doctor sees the patient for a few minutes every day or two and prescribes fixed orders. Much depends on an individual's sensitiveness to pain, his reaction to different drugs, his tolerance for addiction. All of this can only be learned by the day to day hourly observation of the nurse, so that she is in a better position to administer the daily drug care than the doctor is, provided she has an understanding of the various narcotics, and has close coöperation with the medical staff.

A cancer patient can be kept more comfortable, with far less narcotic consumption, in a convalescent service with a few intelligent nurses working in this manner than in a busy general hospital where nurses change frequently, and the care of the patient must be routinized. Small wards, with single rooms, if at all possible, are desirable, because of the frequent terminal symptoms and frequent sudden deterioration and change in the patients condition.

*Bed Sores.* The best therapy for pressure sores is avoidance. A debilitated patient can get an intractable bed sore in one or two days.

General hygiene is important: rub the back (massage), etc. daily; keep sheets taut; avoid crumbs or other particles. Avoid pressure by changing posture frequently, using a water cushion, air mattress, cotton doughnut, pillow under the back or the knees, etc. Avoid maceration of the skin. Absorb discharges by frequent changes of dressings. If the skin is dry, use hydropur wool fat.

For a reddened area we use one of the following techniques:

1. Lather with fels naphtha soap, letting it dry, forming a paste. Keep patient off the part twenty minutes. Repeat twice daily every day for one week or until healed.

2. Paint with 5 per cent silver nitrate, or with collodion.

3. Elastoplast adhesive stretched tightly over the irritated area in two layers at right angles to each other.<sup>4</sup>

For an open ulcer:

1. 5 per cent tannic acid spray until a crust forms.

2. Light cradle. Surgical dusting powder. Keep superficial gangrene dry.

3. Elastoplast, applied as above in two tightly stretched layers placed at right angles to each other and left undisturbed for several days is an excellent method.

*Ulcerated Lesions.* If a bed sore extends, and one has cellulitis and moist gangrene to deal with, dressings should be changed frequently, or the ulcer will spread rapidly. Dead gangrene is debrided when the slough is loose.

Most ulcerated lesions (except bed sores) seen in terminal cancer are in and about the mouth and neck. The others are ulcerated breast cancer (very infrequent, considering the large number of cases), an occasional breaking down inguinal gland mass, or superficial sarcoma or other metastases.

Several recent studies have indicated that the germicidal value of local antiseptics is over-rated; body tissue cells are killed more quickly than are the bacteria. The important thing in the care of infected wounds is that nothing should interfere with the flow of lymph and phagocytic cells outward toward the wound surface. These liberate tryptic ferments which are active in combating septic organisms.

Frequent changes of dressings remove fibrin crusts and coagulated discharges which dam back this flow. Moist boric dressings changed every two to four hours, may do more for the patient's comfort than analgesics or sedatives.

Azochloramid is not as irritating as the older chlorine solutions were. There are several recent favorable reports showing shorter wound healing in series of cases with it than without it.<sup>5</sup> It is not expensive if a quantity of gauze is kept in a closed jar,

and a small amount of azochloramid in triacetin poured over it, as recommended by the manufacturers. A small amount of the oily solution diffuses and spreads through a relatively large surface of gauze. Used continuously, there is occasional wound irritation and on rare occasions an increased liability to hemorrhage. These are not serious objections to its routine use. Within a few days a foul smelling neck wound can be rendered clean and comfortable. As an alternate dressing, simple vaseline dressings are soothing to an open neck or mouth wound. Cleanliness is especially important in mouth cases. A moist boric dressing must be changed frequently to give comfort, especially if there is contamination from mouth discharges. Otherwise it cakes up.

After the discovery that the virtue of maggot therapy of infected wounds lies in the urea excreted by the maggots, it was realized that urine, which contains the same concentration of urea (2 per cent) as is found in maggots, has been used therapeutically for superficial wounds and ulcers since Egyptian times.<sup>6</sup> Many persons can still be found who remember that their grandmothers bathed their childhood boils, chapped hands, styes, etc., with applications of urine. It is a stimulant to granulation tissue proliferation, and in no sense an antiseptic, since organisms grow rapidly in 2 per cent urea solution. We have found it of value especially in extensive ulcerating bed sores in 2 or 5 per cent solution. Urea crystals sprinkled directly into a sloughing wound, as advised by Millar,<sup>7</sup> are helpful in cleaning up a dirty wound. They may become irritating, however.

Another mild deodorant solution is a combination of pine oil U.S.P., linseed oil soap and distilled water marketed under the trade name solupin. It has a cleansing and peptizing (soap) action.

Meleney<sup>8</sup> has shown that the foul-odored mouth infections are due to anaerobic streptococcus plus the spirochetes and other fusiform bacilli of the mouth. This is the bacteriology of many cancer ulcerations

in and about the mouth. Though other oxidizing agents, potassium chlorate, potassium permanganate, sodium perborate are of value, zinc peroxide is much more effective.

A potent product "ZPO medicinal" is now marketed and commercially obtainable. It is heated dry to 140 degrees for four hours in small quantities, then mixed with distilled water to the consistency of cream and applied heavily with an asepto syringe. It may also be used as a mouth wash (diluted, one to four parts water) every three to four hours, ensuring good contact by swabbing crevices, etc., with cotton soaked swabs. A few days of such treatment may make the patient feel tremendously relieved, because of the elimination of anaerobic inflammation.

Another soothing mouth wash is detoxyl. Ordinarily bland mouth washes do not give the comfort these two preparations do, probably because of the heavy infection with anaerobic streptococci.

We have not as yet had the opportunity properly to judge the value of sulfanilamide, but this drug should have a wide field of usefulness in the infections and cellulitis of far advanced cancer—many of which contain beta streptococci infections. It has been recommended for infected carcinoma of the cervix before radium application.

For indurated brawny cellulitis heat should be applied, and watch kept for hidden abscesses: neck, post-maxillary region, breast, pararectal, pelvic region, etc. Hidden abscesses have been mistaken for fixed inoperable tumors, especially in the breast. Adequately draining a hidden abscess may relieve intractable pain in an unsuspected manner.

Macerated skin and irritation from discharges, as in the perineum, colostomy, neck, breast, are not problems if the wounds are cared for as above. If they are, one may use: (1) zinc oxide ointment; (2) tannic acid ointment or spray; (3) vaseline; (4) Aluminum ointment which is recently recommended and most efficacious.

Paint the involved surface with:

Powdered aluminum 1 part  
Zinc oxide ointment U.S.P., 2 parts  
Vaseline q.s.

or

Powdered aluminum  
Facial cold cream q.s. to make soft thin paste.

The patient's skin looks like a household radiator, but it toughens and sheds watery discharges.

*Hemorrhage.* Five to 10 per cent of cancer patients die of hemorrhage. The event is usually dramatic and fatal, and except for the suddenness is often a merciful end. The lower uterine artery in cervical cancer most frequently gives way suddenly. Next come hemorrhages about the mouth and neck—lingual or facial arteries or other branches of the external carotid. Then come pulmonary or mediastinal growths (branches of the pulmonary arteries or the aortic side branches). Intra-abdominal ulcerations, generally into arteries in the omentum, an occasional artery in the thigh or other great vessel of an extremity make up the remainder.

Surgically, an occasional ligation of the lingual or facial artery can be done, but usually the growth has already ulcerated too widely for any surgical maneuvers. Deep x-ray therapy can give considerable palliation in checking hemorrhage, especially in the cervix, rectum and mouth. However, most of these cases have already had all the x-ray therapy they can stand several months before the onset of severe bleeding in the far advanced stage.

Though most hemorrhages are fatal within a few days, frequently the patient recovers, and may live four to six months longer.

General measures we have found of value are: (1) a heavy dose of morphine or H.M.C. repeated in one-half hour with the patient kept deeply in sedation for one to two days (dilaudid does not give deep enough sedation); (2) moccasin snake venom; (3) fibrogen, lung tissue; (4)



neohemoplastin and hemostatic blood derivatives.

Locally the usual custom is to pack tightly with iodoform gauze. Sometimes we pack a profuse vaginal hemorrhage from cervix cancer; sometimes we leave the patient alone and give heavy morphine doses for one to two days. Our clinical impression frequently is that the bleeding stops as well under the latter treatment as the former.

Styptics form a protein precipitate which occludes the lumen of small vessels. They control oozing, but not spurters. Large clots should be removed, since such medicaments must come in contact with bleeding vessels. Other measures are: tannic acid 5 to 10 per cent solution; monsell's salt (ferric subsulfate)—powerful, but leaves a dirty coagulum; granulated sugar, an old remedy, still useful in an emergency; thromboplastin, ox brain tissue cephalin; stipven—viper snake venom,<sup>9</sup> hemostatic erce.

Another old remedy useful occasionally in cervical cancer is acetone. Instill  $\frac{1}{2}$  to 1 ounce of acetone into the vagina through a tubular speculum and hold it in place fifteen to twenty minutes, avoiding skin irritation. Repeat every other day as indicated. Old gynecology texts referred to cures of cervix cancer by this method before the advent of radiation therapy.

*Respiratory Tract Lesions.* The patient can easily be taught to use a suction aspirator with a tracheotomy tube. At frequent intervals, a catheter should be inserted far down the trachea to aspirate the pool of secretions which always collects there.

The chronic cough of pulmonary metastases or chronic bronchitis and bronchiectasis surrounding metastatic masses from pharyngeal ulcerations is difficult to treat. However, except for the discomfort of the chronic cough, it is not very troublesome, as cancer symptoms go. The usual cough remedies do not have much value in our experience. A small dose of dilaudid (gr.  $\frac{1}{32}$ ) allays the cough

reflex and gives temporary relief. This can be repeated. Careful watch for pleural effusions is made. These are usually terminal events, but at times breast cancer metastasizes chiefly in the pleura, and repeated aspirations may keep the patient comfortable for four to six months. X-ray often has considerable palliative value in preventing effusions reforming quickly.

The severe dyspnea of mediastinal growths is likewise hard to treat. After x-ray palliation is ended, there is not much left to offer the patient.

*Abdominal Cancer.* When cancer grows heavily in the abdominal cavity, nausea, anorexia and weakness are the chief symptoms. In our experience liver metastases are not painful. If the mass presses on a hollow viscus or involves the retroperitoneal tissues, there is apt to be pain, but otherwise pain is not a prominent symptom. Much can be done for some of these patients without recourse to narcotics.

1. Bowel hygiene—either enemas or mild laxatives.

2. Control of anemia, if possible. If there is no chronic infection, these patients can be made to feel a good deal better by giving them some iron preparation, such as: reduced iron (capsules gr.  $7\frac{1}{2}$  six times daily), ferrous sulfate (tablets gr. 3 three or four times daily), or iron ammonium citrate (90 gr. daily).

3. Improvement in appetite. Taka diastase is a mild remedy. Insulin, 5 to 10 units before meals is at times very helpful and is being used more and more for debilitated conditions.

4. Vitamin B<sub>1</sub> has recently been shown to have a profound influence on glycogen metabolism in the liver; also it has a close relationship to the extrinsic factor in anemia. It is not stored in the body, and if the supply in the food is insufficient, or the disease causes rapid wasting e.g., tuberculosis, cancer, or increased metabolism, it is used up rapidly. Much temporary improvement in appetite and relief of nausea can frequently be obtained by

two tablets of thiamin chloride (or the whole B complex) three times daily on an empty stomach. It has been used with success for the nausea of radiation sickness.

5. Vomiting and nausea are often due to dehydration. Hypodermoclysis, 750 to 1,000 c.c. daily for three to four days may restore this balance.

6. Ascites is most commonly seen in carcinoma of the ovary, sometimes in carcinoma of the rectum or colon, more rarely in upper abdominal cancer. We have had only very moderate success with the newer diuretics, salyrgan, mercurin, etc., in these cases. Abdominal paracentesis gives some relief, but the fluid soon refills and it is usually a terminal event. X-ray therapy has produced palliation and prevented refilling for several months.

These measures are of course palliative, but they frequently spare morphine for a few to several weeks and make for a much more comfortable and satisfied patient. It is in these cases especially that morphine increases constipation, nausea and anorexia.

*Cervix.* Cervix patients suffer from the offensive discharges and the pain in the back, thighs and lower abdomen. For the discharge, solupin (mentioned above under care of wounds) used as a douche once or twice daily (diluted 1:10) relieves the odor in a high percentage of cases. Another remedy is charcoal and iodoform in equal parts, instilled into the vagina or on a tampon.

For a rectovaginal fistula, if the patient is in fairly good condition (life expectancy perhaps three months) we usually advise abdominal colostomy. The patient is much better off with the abdominal anus, for it can be controlled better than the continuous fecal vaginal discharge, and the irritation of feces in the vagina is avoided.

The bladder fistulae from cervical cancer have been a problem. We have in the past kept these patients comfortable with a complicated arrangement of rubber gauze and sheet pads which the patient changed herself every one-half to one hour. Re-

cently we have used continuous suction through a gauze wick in the vagina attached to a perforated catheter lying outside the vagina.<sup>10</sup>

A wick of gauze is placed 2 or 3 inches into the vagina. Just outside the vagina, on the inner side of the thigh, it is attached to a perforated catheter. A suitable type (Hendrikson) may be purchased, or a few perforations are made in a large tube, or the end of the gauze wick is stuffed into the end of a large tube. The tubing is led over the patient's thigh, to a drain bottle hanging on the bed or on the floor. The exit tube from the bottle is attached to a suction pump, either electrically driven (Stedman) or attached to a water pump (Penberthy Injector) or any other apparatus for producing moderate vacuum suction. The gauze wick is changed daily or as often as necessary.

The back pain will be considered later.

*Bladder and Prostate.* Prostate cases can be made comfortable by transurethral punch operation, which can be repeated. Suprapubic cystotomy often becomes necessary later. Bladder cancer usually requires suprapubic cystotomy because of the violent dysuria.

Regarding the care of cystotomy wounds: the tube should be irrigated frequently (daily or oftener). There may be no leakage around the tube, and no dressings whatsoever required, although this is more apt to be true in prostate than in bladder carcinoma. If there is leakage around the suprapubic catheter, a similar continuous suction, with a gauze wick lying free in the urinary seepage and attached to a perforated catheter will keep the patient dry. We have done bilateral ureterostomy where the bladder was too extensively infiltrated for suprapubic drainage. The pain of dysuria is entirely relieved. The wound may be kept dry by using a small size Foley catheter (No. 18 is the smallest manufactured) which has a distensible balloon fashioned on the outer surface about  $\frac{1}{2}$  inch from the end. This is inflated by air or water through a

separate tube built in alongside the main catheter. If the ureter is or can be dilated at all from back pressure, the catheter end can be introduced, the balloon distended in the ureter just beneath the skin, and a water tight drain obtained. The patient is bedridden and the tube must be changed frequently, but the violent dysuria is gone.

These patients often become dehydrated. Again much comfort can be given by simple forcing of fluids.

*Odors.* The foul odor of terminal cancer comes chiefly from cervix discharges, especially when there is a bladder fistula, other draining urinary wounds, and face, neck or breast wounds which have been neglected. With the above regime, there is very little odor in the wards. Electrically driven deodorizers can be purchased, working on the principle of either sucking air into an exhaust or breaking down the air molecule and liberating ozone.

*Intractable Pain.* The worst cases are those of pain in the back, posterior thigh, and lower abdomen in cervical cancer. This is not due to spinal metastases nor to pressure on large nerve trunks in the pelvis, but probably to irritation of sympathetic nerve plexus endings in the pelvis from the inflamed mass. Elsewhere we have reported our experiences with spinal alcohol injections<sup>11</sup> whose greatest field of usefulness is in just these cases. The vise-like low back pain is almost always relieved—or made so much better that codeine and aspirin three or four times a day will relieve it. There may be some residual low anterior abdominal pain or pain in the region of the coccyx. This may require a second injection placed carefully at a different spinal level.

Spinal metastases from breast cancer similarly respond to alcohol injections, although the result is variable. Deep x-ray therapy may cause breast cancer spinal metastases to recalcify, and complete relief will be obtained for four to eight months. Spinal metastases from prostate cases respond in about 50 to

60 per cent of cases to either x-ray therapy or alcohol injections. The usual procedure is to try x-ray first; after full benefit has been obtained and pain recurs later, spinal alcohol can be given. Spinal alcohol injections can be tried for any intractable pain below the collar bone. The best results are obtained by those who carefully plot out the nerve distribution and afferent pathways from the site of the pain, and inject where these enter the spinal cord. Danger of paralysis of the bladder and rectum can be avoided by slow injection and safe dosage. This treatment has taken the place of cordotomy in reports from several clinics and individual observers. Cordotomy may be done later if indicated and if the life expectancy is sufficient to warrant it.

*Breast Cancer.* Often 25 to 30 per cent of the beds in a terminal cancer service are occupied by breast cancer patients. They show a more variegated terminal picture than those with cancer of other organs. We have seen some of these cases bedridden for eighteen months to two years, with spinal paralysis coming on, then improving somewhat; with cerebral symptoms pronounced to the point of coma, then clearing. Prognosis must be guarded, and indications for therapy met as they arise. The usual cough from chest metastases is not very painful. The vomiting and nausea of intra-abdominal, chiefly liver, extension is treated as above indicated, as is also the pain of spinal metastases. Skin metastases require no treatment. Some remarkable disappearances of bone metastases have been reported following irradiation of the ovaries if the patient still menstruates.<sup>12</sup> We have seen the symptoms of far advanced breast cancer improve coincidentally with the normal menopause being established.

*Palliative Operations and X-ray Therapy.* Many of these patients are dehydrated, suffering from sepsis and liver exhaustion. There is always the liability of unsuspected internal metastases. Before any operation is done for far advanced cancer one should

carefully weigh: (a) the risk involved; (b) the probable life expectancy; and (c) the amount of palliation which the operation will bring. This is especially important in abdominal cancer, where it is not unusual to have a sudden exitus a few days after laparotomy, which comprised only an abdominal incision, a quick exploration and closure. All hospital record rooms have many such charts. A few days clinical hospital observation of these patients, careful estimation of fluid balance, blood chemistry, anemia, etc., will avoid a good many of these occurrences. They do nobody any good. We feel that the chief unsuspected risk comes from an exhausted liver which cannot be estimated clinically before the operation. The risk and potential palliation may be explained to the family and the decision left to them. Sometimes they want everything possible done for the patient; at other times they prefer not to have him "bothered" or "tortured."

Similarly, we have seen many cases where protracted x-ray therapy did no good. Sufficient experience with this valuable therapeutic agent has now accumulated, so that it should be given on more definite indications, and not to every cancer patient to whom nothing else can be offered. It is not entirely harmless. Occasionally the rapid deterioration following x-ray therapy is more than coincidental. Such cases are not numerous, but they occur in the experience of all who see many of these patients.

#### COMMENT

The symptoms complained of during the far advanced stages of cancer depend not upon "general exhaustion," "general debility," "cancer cachexia," etc., but upon the particular pathologic change which cancer produces in the particular organ or body site where it is active. A local ulceration causes sepsis; aspiration of mouth discharges causes bronchitis and bronchiectasis; a hollow viscus may be obstructed or a fistula drain to the exterior from an internal organ. Pain is due to a

variety of pathologic processes. The treatment must seek to differentiate these causes, and be particularized to each of them.

#### SUMMARY

A régime for the care of far advanced cancer patients is elaborated.

The following considerations in therapy are discussed: the psychologic approach; nursing care; bedsores; ulcers; odors; discharges; the peculiarities of abdominal cancer; fistulae from hollow viscera; hemorrhage; intractable pain; palliative operations.

The importance of treating the exact cause of the discomfort rather than loading the patient with narcotics, is emphasized.

#### REFERENCES

1. WILD, R. B. Address on treatment of patients with inoperable cancer. *Lancet*, 2: 1062-1064 (Nov. 24) 1928.
2. HERTZLER, A. E. The Horse and Buggy Doctor. 1938.
3. JACKSON, HENRY, JR., and MINST, G. The medical care of the cancer patient. *Am. J. Cancer*, 15: 8 (Jan.) 1931.
4. CARTY, T. J. A. Treatment of bed sore with elastic adhesive plaster. *Brit. M. J.*, 1: 105-106 (Jan. 18) 1935.
- FANTUS, B. Therapy of Cook County Hospital; therapy of bedsores. *J. A. M. A.*, 104: 46-48 (Jan. 5) 1935.
- FANTUS, B. Advances in therapeutic technic. *J. A. M. A.*, 105: 877-881 (Sept. 14) 1935.
5. FORREST, YOUNG. Treatment of surgical infections with new chlorine solutions. *Surg., Gynec. & Obst.*, 63: 318-324 (Sept.) 1936.
- SUTTON, L. E., and VAN DUYN, JOHN. Treatment of infected wounds with azochloramid. *New York State J. Med.*, 36: 1835-1838 (Dec. 1) 1936.
- KENNEDY, R. H. Use of azochloramid in infected wounds. *Am. J. Surg.*, 31: 294-299, 1936.
6. FOULGER, J. H., and FOSHAY, L. Antiseptic and bactericidal action of urea. *J. Lab. & Clin. Med.*, 20: 1113-1117, 1935.
- ROBINSON, W. Use of urea to stimulate healing in chronic purulent wounds. *Am. J. Surg.*, 33: 192-197 (Aug.) 1936.
- MULDavin, L. F., and HOLTZMANN, J. M. Treatment of infected wounds with urea. *Lancet*, 1: 549-551 (March 5) 1938.
7. MILLAR, W. M. Urea crystals in cancer. *J. A. M. A.*, 100: 1684 (May 27) 1933.
8. MELENEY, F. L. Prophylactic and active use of zinc peroxide in foul smelling mouth and neck infections. *Ann. Surg.*, 107: 32-38 (Jan.) 1938. Bacteriology of amputations. *S. Clin. North America*, 18: 321-328 (April) 1938. Use of zinc

- peroxide in oral surgery. *Internat. J. Orthodont.*, 23: 932-940, (Sept.) 1937.
- MELONEY, F. L., and JOHNSON, B. A. Further laboratory and clinical experiences in treatment of chronic undermining burrowing ulcers with zinc peroxide. *Surgery*, 1: 169-221, (Feb.) 1937.
9. MAC FARLANE, R. G., and BARNETT, BURGESS. Haemostatic possibilities of snake-venom. *Lancet*, 2: 985-987 (Nov. 3) 1934.
- BURGESS, BARNETT. Haemostatic uses of snake venom. *Proc. Roy. Soc. Med.*, 28: 1469-1472, 1935.
10. SALTZSTEIN, H. C. A simple method for keeping bladder fistulas from cervix cancer dry. *Surg., Gynec. & Obst.*, 69: 111-112 (July) 1939.
11. SALTZSTEIN, H. C. Intraspinal (subarachnoid) injection of absolute alcohol for the relief of intractable pain. *Internat. Clin.*, 3: 167-182 (Sept.) 1938.
12. TAYLOR, G. W. Rationale of artificial menopause in carcinoma of breast. *Am. J. Roentgenol.*, 39: 419-421 (March) 1938.
- DRESSER, R. Effect of ovarian irradiation on bone metastases of cancer of the breast. *Am. J. Roentgenol.*, 35: 384-388 (March) 1936.
- CLARKSON, W., and BARKER, A. Five year cures of mammary carcinoma with multiple metastases to bone. *Am. J. Roentgenol.*, 36: 615-621 (Nov.) 1936.



CAUSALGIA is not an organic disease, but a functional one. It seems to be brought about by vaso-motor disturbances at the site of any wound whatever, whether affecting the connective or muscular tissues, the adventitia of an artery or vein, or the supporting connective tissues of a nerve.

From—"Surgery of Pain" by René Leriche (Williams and Wilkins).

# PROTRUDING EARS: A METHOD OF PLASTIC CORRECTION

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**A**MONG the most engaging of purely plastic surgical problems is the correction of protruding deformities of the ears. (Figs. 1 and 2.) There is a certain degree of fascination in transforming such a deformed auricle from a state of distortion to one of normalcy, the result of which not only improves the general appearance of the patient, but also, in turn, often agreeably alters his mental outlook and emotional stability. It is interesting and instructive to review the procedures which have been advocated in years past for the repair of such deformities, and to discover that by a process of trial and error the surgical technique has undergone a series of gradual steps toward perfection. Although, year after year, new details of technique have been proposed which have elevated these operations from a state of crude experimentation to accomplished attainments, it must be admitted by all that surgical methods of the present day for the correction of protruding deformities of the ears still are not in a final stage of faultlessness. There is yet opportunity for improvement.

A protruding deformity of an ear in itself is a trivial matter, but the detrimental effect of such a deformity on the personality of some individuals is extremely significant. If such a malformation does not induce an actual obsession, in many instances it produces an exaggerated feeling of inferiority with all the attendant and subsequent complications usually associated with such a sense of inadequacy. Few of us realize the amount of mental discomfort endured by some sensitive individuals who have abnormalities such as this, and few appreciate the satisfaction of mind which these people gain by a plastic adjustment of this unnatural conformation of the

ears. When this deformity is the fundamental basis for an obsession or an inferiority complex, correction of the abnormality promptly removes the mental or emotional symptoms. Even assuming that a deformity such as the one under consideration has produced no mental symptoms whatever, there is nothing incredible in the fact that a person with severely protruding ears should wish to improve his personal appearance. Then, too, it is a matter of common knowledge that even a few intelligent and well-educated people find it impossible to obtain certain types of positions because of this deformity. Consequently, it is indeed fortunate for many individuals that plastic procedures have been developed for the correction of such deformities.

An outstanding ear is the result of a congenital malformation of the anthelix. Normally, the contour of this part of the auricle is convex as viewed from its ventral surface. (Fig. 3.) It is this marked convexity of the cartilaginous anthelix that bends the scaphoid and helical portions of the ear inward toward the head and prevents their protrusion. (Fig. 4.) In an outstanding ear, however, the anthelix is flattened or actually concave, and the helix of necessity stands away from the head. (Fig. 5.) What embryologic factors produce this flattening or concavity of the anthelix are unknown. To make a broad statement, it might be said that the cephalo-auricular angle is decreased in proportion to the increase of convexity of the anthelix.

This generalization, as a matter of fact, forms the basis of treatment in the more recently devised operations for the correction of outstanding ears; the aim of these surgical procedures is to restore to the anthelix its normal convexity, which, in

turn, mechanically deflects the ear inward toward the head. This is usually accomplished by incising the auricular cartilages

entering school, so as to preclude the possibility of his developing emotional disturbances as a result of the abnormality.

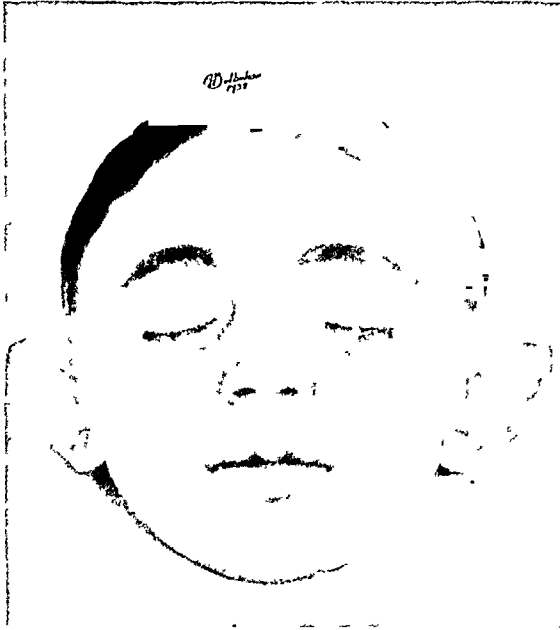


FIG. 1. Wax mouldage of a patient with a marked degree of protrusion of the ears.

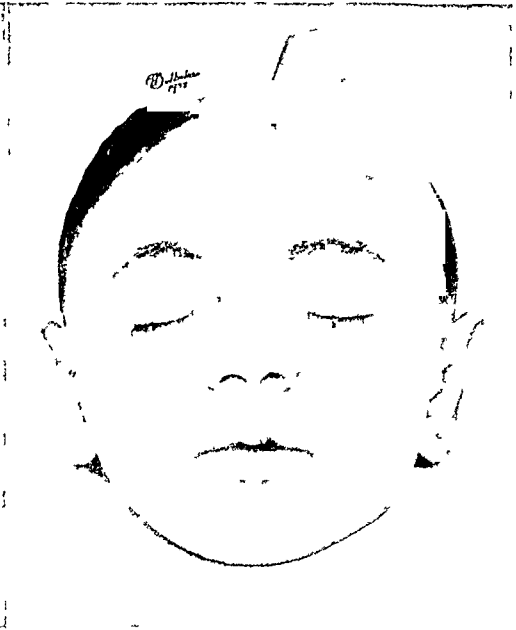


FIG. 2. Wax mouldage of the same patient after a plastic reconstruction of the ears.

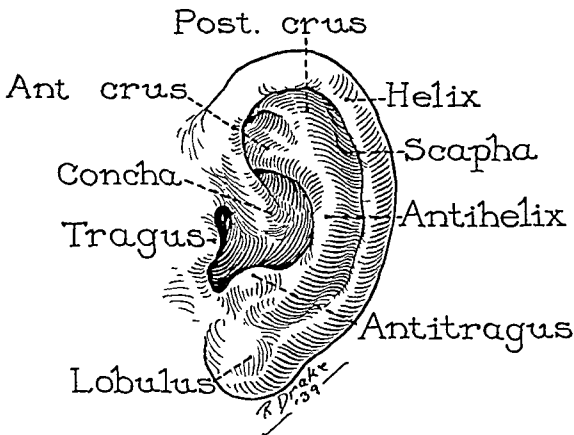


FIG. 3. A normal ear demonstrating the convexity of the anthelix and its posterior crus.

in a vertical direction along the line of the anthelix. Then by folding the cartilage and suturing the cut edges the parts lie side by side (Fig. 6), and the protruding appearance of the ear is remedied.

This malformation is bilateral in most cases. It is a deformity which can be corrected satisfactorily at almost any age. A child with outstanding ears is best operated on when he is about 5 years old, before

Such operations at this early age apparently do not interfere with the subsequent normal growth of the ears.

We wish to describe a method which we have devised for the plastic correction of abnormally protruding ears. In many respects, the technique of this operation is similar to that set forth by others; the principal point of difference lies in the manner of inserting the sutures which form or mould the anthelix. Although we do not wish to discredit other methods, we are of the opinion that our plan has two advantages over other procedures. First, it permits of bending the auricle backward to any desired extent as a final step in the operation even after the wound has been completely closed. Second, it facilitates establishment of the same cephalo-auricular angle on each side when the deformity is bilateral.

Although the details of this operation are, except in the method of suturing, somewhat analogous to those outlined by Davis and Kitlowski,<sup>1</sup> and by MacCollum,<sup>2</sup> there are enough minor variations to warrant

giving a full account and description of the technique which we employ.

In performing an operation for protrud-

renalin is injected subcutaneously on both the anterior and posterior auricular surfaces for hemostasis. An elliptical piece of

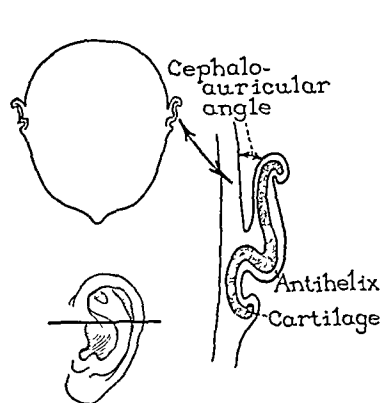


FIG. 4.

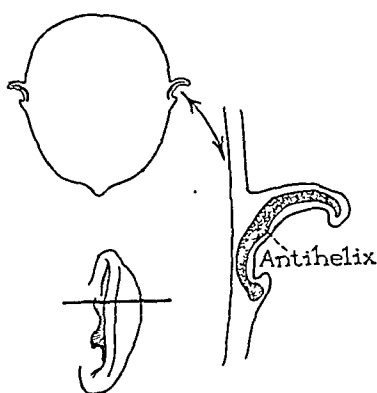


FIG. 5.

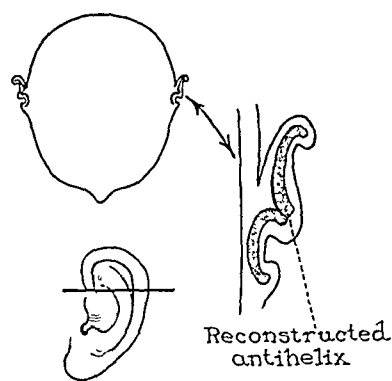


FIG. 6.

FIG. 4. Cross section of a normal ear illustrating the marked convexity of the anthelix.

FIG. 5. Cross section of an outstanding ear illustrating the flattened anthelix and the resultant protrusion of the scaphoid and helical portions of the auricle.

FIG. 6. Cross section of a reconstructed protruding ear. After excising an elliptical strip of cartilage, correctly inserted mattress sutures evert the cut edges of the cartilage so as to produce a normally convex anthelix, which, in turn, rectifies the abnormal state of protrusion.

ing ears, many surgeons prefer to place the patient in a prone position on the operating table. However, since by our method the ears are tied back as a final step in the plastic procedure, we believe that it is advantageous to have the patient on his back; this permits a full view of the face so that one can judge best whether or not the relative final position of the two ears is symmetrical.

The hair is shaved for a distance of about 1 inch away from the ears, and the patient is anesthetized by the intratracheal method, employing nitrous oxide, gas and ether. The auricles are then painted with tincture of merthiolate, and sterile towels are draped about the patient, leaving both ears exposed. Even when the deformity is unilateral, it is well to leave the uninvolved ear uncovered for comparison with the malformed member. By proper arrangements, the towel which covers the front part of the head may be turned down, thus permitting inspection of the entire face at any time.

Before incising the skin, the proposed position for the anthelix is outlined with an indelible pencil on the anterior aspect of each ear, and novocaine containing ad-

skin which includes the sulcus formed by the junction of the auricle with the head, is excised from the dorsal surface of the ear. (Fig. 7.) At its greatest width this strip of skin measures about 1 cm. In a vertical direction, this excision of skin should be extended from the point at which the helix joins the temporal region to the lobule below.

By undermining and reflecting the cutaneous margins of the wound, an excellent exposure of the dorsal surfaces of the auricular cartilages is obtainable. With the aid of a hypodermic needle dipped in methylene blue, the position of the anthelix as previously outlined in pencil on the ventral surface of the ear can be transferred to the cartilage. This is accomplished by repeatedly thrusting the needle through the full thickness of the ear along the pencil-drawn line of the anthelix. As a result of this procedure, a series of blue spots is produced on the exposed surface of the cartilage. (Fig. 7.) This row of dots serves as a guide for the excision of an elliptical piece of cartilage which at its widest point should not exceed 5 mm. (Fig. 7.) A small scalpel and periosteal elevators are employed in removing the cartilage.



It is of the utmost importance in this operation to make certain that the excised strip of cartilage extends the entire length

process of shaving. He claims satisfactory results from this procedure.

Complete hemostasis is a valuable aid

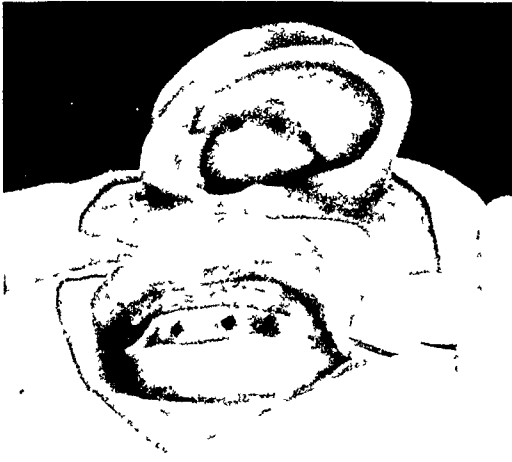


FIG. 7. Wax mouldage of a protruding ear as seen from its posterior surface. The anterior auricular surface, which is visible, is a mirror image. In order to expose the cartilage, the skin is incised and reflected as illustrated. The series of dots marks the proposed position for the anthelix. One may note the outline of the elliptical strip of cartilage, which is being excised.

of the ear actually to divide the auricular cartilages into two separate and distinct parts. Even a small bridge of cartilage remaining between these two cartilaginous parts possesses an elastic force sufficient to restore the ear more or less completely to its original form. On examination of a microscopic section of the full thickness of the ear, it is amazing to observe the abundance of elastic fibers that lie in every direction within the cartilage and perichondrium. There is little wonder that an ear will resume its original shape unless the cartilage is completely severed. Rather than remove an elliptical piece of cartilage, some surgeons prefer merely to incise the cartilage along the line of the anthelix. However, in our experience, the ear can be folded back with greater ease if a narrow strip of cartilage is excised.

Through personal communication, we understand that J. P. Webster does not incise the cartilage but merely reduces its thickness in the region of the anthelix by a

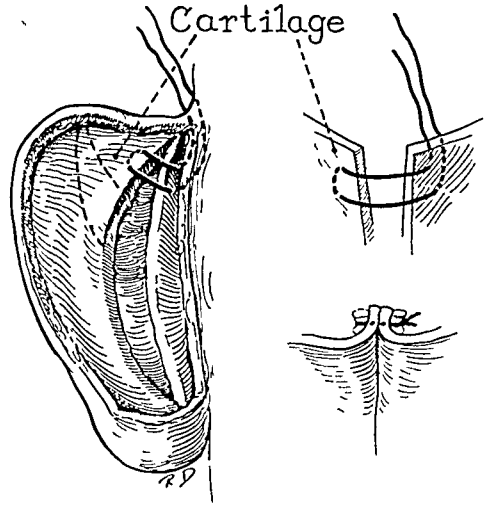


FIG. 8. Diagram of the posterior surface of a protruding ear. The skin has been entirely removed to give a better view of the auricular cartilages. This drawing illustrates the elliptical strip of cartilage which has been removed, and the method of inserting mattress sutures from the anterior surface of the ear through skin and cartilage. On tying these sutures over small cotton rolls, the cut edges of the cartilage are everted to produce a convex anthelix. The dotted margins of the triangular area on the upper portion of the auricular cartilage indicate the site at which a secondary wedge of cartilage may be removed for the construction of a convex posterior crus; this procedure counteracts any tendency of the upper portion of the ear to flop forward.

toward prompt healing of the wound. Before suturing, much care is taken to insure a dry wound by ligating every vessel which may continue to ooze. Mattress sutures are next inserted. Usually, four in each ear are required, and white silk is the preferred suturing material because of its strength. Each mattress suture is introduced from the anterior aspect of the ear, through the skin and cartilage and across the cut edges of the cartilage posteriorly.

The course of these sutures through the ear can be explained more intelligibly by means of diagrams (Figs. 8 and 9) than by a written description. Although inserted at this stage of the operation, these sutures are left untied until the cutaneous edges

of the wound are carefully approximated with interrupted fine black silk sutures. Following this closure of the wound, the

of the ears is governed by the degree of tension placed on the mattress sutures when tied. It is well to remember that the



FIG. 9. Wax mouldage of a protruding ear. The anterior surface is a mirror image. The method of inserting a mattress suture from the anterior auricular surface through skin and cartilage is demonstrated.



FIG. 10. Wax mouldage of a protruding ear. The anterior surface is a mirror image. The manner in which the mattress sutures are tied over cotton rolls after the cutaneous incision has been closed with interrupted silk sutures is demonstrated. Notice the marked convexity of the anthelix produced by tying these mattress sutures and how the ear is folded in toward the head.

mattress sutures are tied firmly over small cotton rolls. (Figs. 10 and 11.) The tying of these sutures effects the following results:

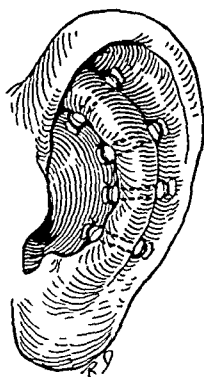


FIG. 11.

FIG. 11. Diagram of a reconstructed protruding ear with mattress sutures in position and tied over small cotton rolls. A marked degree of convexity of the anthelix has been attained by this procedure, and the deformity of the ear accordingly has been corrected.



FIG. 12.

FIG. 12. Diagram of a reconstructed protruding ear in which the convexity of both the anthelix and the posterior crus have been increased, the latter to overcome any tendency of the upper portion of the ear to lop forward. Necessary mattress sutures are in position.

the cut edges of the cartilage are everted and brought together side by side; this produces a convex anthelix, which, in turn, rotates the scaphoid and helical portions of the ear inwardly so as to correct the deformity. The amount of inward deflection

normal cephalo-auricular angle should be about 30 degrees. In some cases, it is desirable to expose the face and tie the mattress sutures in each ear simultaneously; this insures a symmetrical alignment of the two ears.

It is our opinion that external mattress sutures offer a more effective means of forming the anthelix than do subcutaneous catgut sutures. If the latter are employed, after the cutaneous edges have been sutured, there is no possible way of adjusting the position of the ear without opening the wound. Furthermore, such catgut sutures occasionally become absorbed before the healing process is complete; should an infection of low grade occur, the catgut will disintegrate when, perhaps, its tension is most desirable. The use of white silk mattress sutures obviates such complications.

On completion of the operation, sterile gauze is lightly packed into the convolutions of the ears and a firm head bandage is applied. Four or five days later, the bandage is temporarily removed while the black silk skin sutures are taken out. About three weeks after the operation, the bandage and mattress sutures are removed, and the patient is instructed to maintain pressure on his ears with adhesive tape for at least another two weeks. After this length of time, there is no danger of the ears reverting to their original distorted state.

In the majority of cases of protruding ears, the technique as described will correct the deformity very satisfactorily. However, in a few instances, the uppermost portion of the ear tends to lop over through the scaphoid region, and no amount of tension on the mattress sutures will overcome this limp, hanging tendency, which greatly impairs the final cosmetic result. Examina-

tion of a normal anthelix reveals a markedly convex posterior crus which passes directly upward with a slight forward inclination. Any congenital flattening of this anatomic division of the auricle permits the upper pole of the ear to lop forward. Correction of this deformity is possible by accentuating the convexity of the posterior crus. When removing the elliptical piece of cartilage to form the new anthelix, a secondary small strip can be excised in the region of the posterior crus. (Fig. 8.) One or two mattress sutures properly placed will increase markedly its convexity and this, in turn, will fold the drooping portion of the ear back into a more normal position. (Fig. 12.)

#### CONCLUSION

The successful correction of outstanding ears depends on many factors, but primarily on a careful preliminary inspection of the ears, especially in reference to the anthelix and its posterior crus, and a foreseeing plan of treatment in each individual case. In our experience, it would seem that the more perfectly one can mould such a distorted auricle to conform to the normal, the more certainly can one anticipate a satisfactory result.

#### REFERENCES

1. DAVIS, J. S., and KITLOWSKI, E. A. Abnormal prominence of the ears—a method of readjustment. *Surgery*, 2: 835-848 (Dec.) 1937.
2. MACCOLLUM, D. W. The lop ear. *J. A. M. A.*, 110: 1427-1430 (Apr. 30) 1938.



# SEVERE INJURIES OF THE FACE

## SOME CONSIDERATIONS IN THEIR DIAGNOSIS AND TREATMENT

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THE purpose of this article is to present some principles in diagnosis and a discussion of some indications for treatment which should be routinely followed in injuries of the face. Several experiences in maltreatment and careless routine neglect of patients have led to these suggestions on this subject. Entirely competent physicians seem to be at times unaware of their responsibilities in complicated cases.

When a physician takes on the responsibility of treating traumatic cases, he must have had a minimum of training to satisfy the requirements of the state, national, and often the workmen's compensation laws. The average doctor, however, does not always have sufficient graduate training to qualify him as a specialist in general surgery, traumatic surgery, eye, ear, nose, and throat surgery, brain and nervous system surgery—all combined. In many cases it is to the advantage of the patient to have the neuro-surgeon, eye and ear man, general surgeon and reconstructive surgeon join forces.

### EYE INJURIES

As a result of this lack of training there is probably no greater error than superficial inspection of eye injuries, even though no visible laceration is at first suspected. It is of utmost importance to diagnose the condition of the interior of the orbit as well as merely to observe, let us say, a slight ecchymosis of the lower lid. Intelligent patients may help in the diagnosis of difficult conditions by remarks about loss of vision in this or that quadrant. They may report a "hazy blur" instead of the usual clear vision. This may suggest anything from a dislocated lens to a detach-

ment of the retina, or hemorrhage into the vitreous from a ruptured sclera and deeper layers of the eye.

On the other hand, a patient who has partly lost consciousness or who is in shock due to other more pressing injuries, may neglect to mention his half blind eye, or not notice it himself until long after the injury. Any injury to the face should therefore warrant an eye examination sufficient to prove good function, allow visualization of the fundus, and permit a gross estimate of the intraocular tension. It is not well enough known that even light blows on the eye or head may damage the eye, although nothing is suspected either by the coöperative patient or the examiner until several hours or days later.

A neglected patient who never knew he had a hemorrhage behind the retina, a dislocated lens, or a traumatic cataract may not associate trauma with the gradual decrease in vision of one eye until some days or months later. It may be years before an observing individual notices that one eye looks a little queer and seems at times to "wander" or "cross" with the other eye. So many of these cases are seen by eye specialists years after the original injury, that it is small wonder that the general surgeon never hears much about the part he and his colleagues may have unwittingly played in neglecting to diagnose the original lesion.

Seemingly mild external wounds may accompany severe internal hemorrhage or disruption of the retina and ciliary body.<sup>2</sup> The time to insure proper care is immediately after the accident, and not a day or two later when the ophthalmologist makes rounds. Small piercing wounds within the cornea or near the limbus are so productive

of serious loss of useful vision after they are healed, that no time should be wasted in securing accurate diagnostic and therapeutic aid.<sup>3,4</sup> Every case of facial injury should be examined as if there might be a detached retina, a puncture of the sclera, internal eye hemorrhage, or other serious damage. Outside help may then be necessary, unless the examination is complete enough to warrant a safe prognosis.

The diagnosis of most eye injuries is not really difficult. Some knowledge of the use of the ophthalmoscope is indispensable and some idea of how to test vision grossly is a requirement. The fact that a blow over the supraorbital ridge will sometimes affect the superior oblique muscle by concussion or other more severe injury, makes observation of the patient's ability to move the eyes together, an important part of the diagnostic examination. If both eyes work well together, and the fundi are clear, pupils equal, round, regular, reacting alike to light and accommodation; if the tension is normal to palpation; if no tenderness is noted; and if, in addition, each eye registers  $20/20$  vision with the Snellen test charts, the chances are that no serious eye injury has occurred.

Testing of the intraocular tension by pressing on the upper lid over the eyeball rules out loss of vitreous or crushing of an eye, with a rupture of the sclera.

Even a ruined eye does not warrant neglect. The eye may be completely useless in function, and may never get back even a fraction of useful vision, but it must be prevented from harming the good eye. Sympathetic ophthalmia has been known to produce serious harm in an originally normal opposite eye.<sup>3,4</sup> Many regard this disease as a myth, and never learn that the unaffected eye must be watched for the slightest suspicion of photophobia, lacrimation, and beginning circumcorneal injection. These signs are possible indications for radical enucleation of the traumatized eye or other therapy. Sympathetic ophthalmia is not extremely rare.<sup>3</sup> Any wounds in the region of the cornea, through the sclera, or

even behind the eye-ball itself may bring about this reaction in the good eye, sometimes resulting in its ultimate loss.

Traumatic corneal ulcers, which may result from family fights, are not apparent to the inexperienced observer. The spasm of the lids is often so great that many a doctor may say, "Use an icebag and come back tomorrow," if he cannot get the spastic lids open long enough to see much under them. If a fingernail has scratched the cornea in such a case, and the examiner does not know the importance of early correct treatment, infection may set in and an iritis, cyclitis, and possible panophthalmia get under way, guaranteeing complete loss of the eye.

Corneal ulceration should be suspected when there is great eyelid spasm after a direct injury. The diagnosis is simple after anesthetization of the conjunctiva with cocaine or other local anesthetic. The best way to see the ulcer is by the instillation of a drop of fluorescein followed by immediate irrigation of the conjunctiva with boric acid solution. If an ulcer is present, it will stain greenish yellow because of the affinity of the dye for the denuded surface of the cornea where the ulcer is present.

The treatment of corneal ulcer is simple when the diagnosis is prompt and when perforation through the anterior chamber has not occurred. Otherwise it is a most serious injury. The pupil should be kept dilated by atropine, and the eye covered; daily dressings with indicated medications are necessary.

If the trochlea is non-functioning and the superior oblique muscle is not taking part in the extraocular movements, the finding should be recorded but does not necessarily alter the immediate treatment. Later malfunction of the external ocular movements may be explained if the inability of the patient to move the eye upward and outward or downward and inward, is noted and believed to date from the original trauma to the face. Loss of ability to rotate the eye externally after trauma indicates injury to the abducens nerve, often sug-

gesting a basal skull fracture, and is commonly seen in supposedly mild head injuries.

Subconjunctival hemorrhages cause alarm in patients and may be serious indications of severe skull fracture. To differentiate the slight from the serious, a complete physical and neurologic examination as for suspected skull fracture is necessary. A complete eye examination will rule out other injuries inside the eye. Prognosis cannot be given until the patient states and proves his ability to see well. Subconjunctival hemorrhage either on the upper or lower part of the sclera is interpreted much more seriously if there is blindness in both eyes after an awakening from coma, or if a depressed skull fracture through the occipital areas, over the visual association centers, is also present, as occurs in rare instances.

Lacerations in the region of the eye, especially of the upper lid, can be very serious because (1) the likelihood of infection is multiplied many times with puncture wounds, and (2) there is the possibility of a sharp foreign body's having perforated either the eyeball or skull. A case has been reported where the patient himself did not realize that when he fell, he had run an ice pick an amazing distance into his head without serious immediate symptoms. A good history, accurate examination, and x-ray if doubt exists, will disclose the diagnosis and probable outcome.

#### NOSE INJURIES

The diagnosis of air in the subcutaneous tissues may suggest to the examiner that the paranasal sinuses have been ruptured. If a patient is struck on the nose, develops a nose-bleed, and then "blows up his eye" in trying to get the blood out of his nose, this suggests ethmoid fracture. Such a case should be treated as a potentially serious one, since the ethmoid is a bone of the skull and meningitis can follow such a fracture.

Often the patient who lacrimates considerably after an injury to the face, either blunt or lacerated, suggests to the examiner

that his eye bothers him. Examinations with all due care, reveal no eye lesion. He may, however, have a ruptured nasolacrimal duct or an obstructed duct due to swelling of the inferior turbinate from the nose injury. A simple test to determine the patency of the duct is to drop a little mercurochrome on the lower eyelid of the lacrimating eye and then ask the patient to blow his breath gently out through the nose without much force and without compressing the other nostril. The dye can be seen on the handkerchief provided the injury has not entirely occluded the duct. This test is not to be tried when there is any nose hemorrhage. In many face injuries the test can be of aid in pointing out the intranasal swelling and a more serious condition than may have been at first suspected. The ever-present medicolegal aspects may thus be foreseen and obviated.

If a doctor makes a diagnosis of injury to the duct before the patient leaves the hospital and tells him what the outcome is likely to be, there is usually no trouble. If, on the other hand, the patient leaves the hospital believing that his lacrimating eye is supposed to improve and that there is nothing really wrong with it, he may later institute a suit for malpractice. The fact that many of these cases of injury to the nasolacrimal duct improve spontaneously is no excuse to neglect diagnosis.

#### WOUND SUTURE

In deciding which cases need suturing of lacerations and which may heal without sutures, the individual patient, the accessibility of good operative assistance and the judgment of the operator are all important.

Extensive, bleeding wounds certainly require suture. The indications for suturing multiple small laceration-contusions and perforations of the face from splintered glass, as in auto accidents, are less certain.

One must consider what functions will be lost if the face wounds are not repaired and whether a competent repair of the face lacerations will delay or hinder the progress of recovery of possible injuries elsewhere.

Normally, the most important facial functions are those having to do with (1) sight, (2) movements of all the muscles of facial expression, opening and closing the eyelids, (3) moving the eyes, (4) chewing, (5) lacrimating, and (6) salivating normally, (7) hearing (part of it has a bearing on the external ear), (8) breathing normally through the nose, and finally, (9) making a presentable "cosmetic" appearance.

Can a clean, small laceration across the nasolacrimal duct, at the inner canthus of one eye, a jagged wound of the forehead, and a gaping wound of the angle of the mouth—all be left untouched, unsutured and untreated because the patient is a little "dizzy" from the force of the accident? The answer is "yes," but the result would be poorer than a clean repair and accurate approximation by the best plastic technique. Reference to the injured functions in this case shows why suturing should be done.

To begin with, the forehead has possibly two functions impaired, that of taking part in facial expression (if the eyebrow cannot be elevated), and that of sharing in the appearance at rest. Next, closer examination of the inner canthus may show that without suture, the duct opening may not heal in its normal location, and that the tears may run down the face instead of into the duct. The gaping wound of the mouth may result in the loss of one or more of several functions: (1) normal "cosmetic" appearance at rest, (2) normal expression during talk, (3) normal appearance during eating, (4) normal closure of the mouth.

Everyone realizes the importance of such injuries when all the labels are put on the lacerations of this hypothetical case. Few take the trouble to make a detailed diagnosis of facial injuries when they are first seen. I feel strongly that facial injuries are emergencies, often of as much significance as a ruptured spleen or ruptured appendix. A ruptured spleen is difficult of diagnosis and of major impor-

tance as to life or death. However, where intra-abdominal hemorrhage from rupture of the spleen is suspected, the doctor is awake to his responsibility because of the imminent risk of death. I plead for preservation of the patient's facial *functions* for all the rest of his days. The difficulties may be undervalued at the first examination after injury.

Hemorrhage in neglected face injury cases is equally important. Secondary hemorrhages are common after improperly treated nose fractures, and especially in infected deep wounds, which are not sutured.

No patient with facial wounds should be put under observation in a hospital without an exact recording of the wounds as to depth and extent. Too often a patient is neglected because no one troubles to examine the wounds aseptically for fear of starting more bleeding and having to tie off more bleeding vessels. Such practice is entirely wrong. Every wound ought to be examined carefully, shaving the head if necessary. One must scrub the dried crusts off to find the end of the laceration and see where the depth of the skin cut leads.

It is better to stop bleeding on the examining table when a nurse can help with suture material than it is to stop a secondary hemorrhage later on, or watch a massive infection develop in retained blood clots which could better have been removed at the first examination and which could have been avoided in careful fashion by early suture.

Too many competent surgeons feel that a 2 inch cut surface is "small stuff," rather beneath their dignity. They put in only one or two stitches, if any. The careful plastic surgeon, on the other hand, may spend an hour or more repairing a 3 or 4 inch wound on the face. If the general surgeon feels that accepted methods of prevention of over-scarring can be omitted from his treatment of lacerations, he should confine his surgery to the covered parts of the body (which today are becoming rather restricted). Long experience is the only safe guide by

which to limit the amount of suturing of wounds of the face.

Hemostasis comes first. I ask patients to take a deep breath and hold it, when this is safe, so that when I sponge in facial wounds, I can see evidence of venous ooze. It is then possible to clamp and tie.

I recommend starting to suture all face wounds when other more important diagnoses are under control (profound shock, severe hemorrhage, internal injuries, coma, skull fracture, etc.), continuing the suturing in any one wound only long enough to get good hemostasis and accurate approximation of the functioning structures, including the skin. Sometimes after I have repaired a number of face wounds I go over them, adding or removing a suture and putting in two or three more. Often I find I have taken a long time and at other times I find I have done a quick repair.

When the operator learns to classify immediate emergencies as different from future emergencies, he will do better by the patient. An ugly scar because of a contraction of face or eyelid which results in unemployment is a *future emergency*.

#### DIAGNOSIS

Where facial injuries exist, one must exclude in differential diagnosis skull fracture, concussion of the brain, dislocations of the cervical spines and one must consider possible later complications, gas bacillus infection, tetanus, rabies, and erysipelas; embolism, meningitis, sinusitis; tooth injuries, fractures of the upper jaw, fractures of the lower jaw, osteomyelitis, abscess formation in the lymph nodes, cellulitis, Ludwig's angina; loss of hair (eyebrows, hair line of scalp and scalp), retention of foreign bodies under the skin and resulting infections or swellings, and rarely, even staining of the tissues (as from the use of argyrol in the eye, gun-powder, dirt, carbon and other stains).

#### INFECTION AND HEALING

Cellulitis following injuries to the face is sufficiently common to suggest important

hints toward making the diagnosis. Most commonly the inflammation begins on either cheek, or over the bridge of the nose, after fractures of the outer table of the frontal sinuses, rupture of the lateral cartilages of the nasal bones, or bad fractures of the nasal bones. It is also a common complication of a blow on the cheek of an individual suffering from chronic or subacute maxillary sinusitis. Diagnosis is easy when the case is advanced, but treatment is difficult and involved, requiring thorough study and individualization.

One case of infection of the upper lip developing into cellulitis; one infected venous thrombus leading to the base of the brain, resulting in fatal cavernous sinus thrombosis and general sepsis—can prove how important any wound of the face may be. The practice of many surgeons, doing as little to face wounds as is absolutely necessary where they suspect infection, is good teaching. Too much suturing or suturing without drainage can do harm. The possibility of introduction of organisms into the wounds must be kept in mind.

Infection following externally visible wounds of the face can be understood simply because of the obvious likelihood of introduction of foreign material by the object causing the wound. The surgeon should remember that possibilities for severe infection in such wounds will depend upon: (1) the amount and kind of germs introduced; (2) the amount of retained blood clot; (3) the duration of the time before suture and debridement repair are possible; (4) the extent of anemia from loss of blood; (5) the degree of manipulation; and (6) the amount of exposed tissues, and (7) the type of tissues exposed by the wound. The same principles of wound healing apply for face wounds, as in healing elsewhere in the body, with a few possible exceptions.

The most important of these is, when no infection occurs, that healing is more rapid over the stationary parts of the face than in the movable regions as, say, the



corner of the mouth, angle of the jaw, or upper lid. Further, facial wounds heal faster than do wounds in most parts of the body not having so rich a blood supply. The tip of the nose has excellent arterial supply, but a somewhat incompetent venous drainage when extensive lacerations are present. Considerable swelling therefore occurs postoperatively if there is only partial hemostasis. The drainage from the tip is poor when lacerations extend through it so far as to cut off easy lymphatic and venous drainage. This is also the case with the upper lip but not with all other parts of the face, for example vertical lacerations of the chin, cheeks or forehead. The eyelids often have remarkable swelling and distention with lymph and venous ecchymosis. Postoperative swelling is often lessened in such cases by continuous wet soaks of a saturated alum acetate solution.

Infection follows often in the path of tightly closed wounds about the eyelids, tip of nose, and upper lip, where post-operative swelling from edema, blood clot and serum develops. No germs from the outside need be introduced to get such unfortunate results. There are enough staphylococci in the sebaceous glands and on the face to predispose to infection.

Particular emphasis is needed with regard to gas bacillus infections around the face. They are rare but when present are rapidly fatal. They are seen sometimes from no worse wounds than severe, abraded contusions of the cheek and forehead, occurring usually after a fall in the street or on earth contaminated with animal excreta. The same is true of tetanus and all the organisms of the spore-forming, anaerobic group. It is, therefore, of the greatest significance when the patient tells that he was horseback riding and fell on a bridle path, or that he was struck down in the street and slid along on his face.

All wounds are likely to be infected about the face when they are characterized either by severity, by being of the puncture type or by having been subject to probable contamination. Fortunately many show

remarkable healing in the worst cases imaginable, although others are often so rapidly fatal that the attendant cannot prevent rapid complications nor even foresee the likely demise. The poor outcome may be hastened by too much manipulation, tight suture, neglect of systemic hemorrhage, lack of drainage, too tight bandaging, too infrequent inspection of wounds; by neglecting to remove sutures to allow escape of serum and entrance of air when needed; and by the introduction of even slight infection at the time the original suture is performed.

Many doctors fall into habits in technique and that of not using gloves in suturing face wounds has been observed as late as 1939 in certain accident rooms of large hospitals. Certain ophthalmologists have never worn gloves for any of their eye operations. This seems grounds for malpractice suit, since it is common knowledge that the human skin cannot be entirely sterilized. The excuse given is that the touch is better when gloves are not used. They say too that the patient's resistance to infection is good about the eye.

The recognition of an obvious complication of an open face wound—meningitis—is not difficult if the doctor sees the meninges at the time he sews up the forehead and then watches the classical findings of meningitis develop. Sometimes, however, the wound in the coverings of the brain is not visible and hence there is delay in or a missed diagnosis.

If a doctor hears the words "compound fracture of the femur" he realizes that the condition is serious. Yet a tap on the nose, with no outside wound visible, may cause a compound fracture of the nasal bones because the air can reach the fracture through a break in the mucous membrane inside the nose. The same is true of many fractured lower jaws, upper jaws, loss of teeth from trauma, and also forehead and ear region injuries. External wounds seldom help in diagnosis. Therein lies the greatest danger of wrong treatment.

A bloody nose, bleeding ear, or bloody sputum after injury, may indicate "compound fracture."

A depressed fracture of the outer table of the frontal sinus with only slight swelling of the skin and subcutaneous tissues, should be understood as a "compound fracture," because air through the nostrils is in continuity with the broken bone. Why is this not more commonly taught and appreciated?

The diagnosis of "fracture of the outer table of the frontal bone" is likely to be more significant than some think, if the possibility of air-borne infection is realized by the route mentioned above. So, therefore, should the serious likelihood of infection of the meninges, with resulting meningitis, be remembered. No wound involving a compound fracture of the skull should be sutured except in the main operating room under strict technique.

#### CONCLUSIONS

There are no set rules by which a surgeon can be considered well trained to care for any complicated injury of the face unless he has had more than the usual training given to develop "general surgeons" in some institutions.

Too little is taught about the "functions" of the face and the importance of detailed diagnosis of injuries about the face. The reason for neglect in this teaching is the existence of the overlapping specialties of neurosurgery, eye, ear, nose and throat, oral, general, plastic, and other classifications of surgery.

Some of the conditions mentioned in this paper should lead to better recognition of the wide knowledge and great responsibility assumed by the doctor who accepts the care of facial injuries.

Education of laymen will soon enough remove from the inadequately prepared "specialists," their imagined prerogative of watchful waiting when real knowledge may often indicate immediate, and truly specialized, procedures. Injured people will eventually demand the services of the well trained surgeon.

#### SUMMARY

There has been presented some evidence that wounds of the face are sometimes neglected or inadequately treated because many details of diagnosis are not revealed by casual inspection of facial wounds. A few hints are given for the purpose of reviewing what may be obvious to the traumatic surgeon of wide experience. Exhaustive detail in diagnosis and treatment has been purposely omitted.

#### REFERENCES

1. BLALOCK, J. C. Early care of injuries. Elements of first importance. *Indus. Med.*, 7: 241-243 (May) 1938.
2. DRUCKMANN, E. Retinal detachment and indirect trauma. *Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch.*, 51: 304-328, 1936.
3. TROWBRIDGE, D. H., JR. Clinical and pathological factors in 32 cases of sympathetic ophthalmia. *Am. J. Ophth.*, 20: 135-148 (Feb.) 1937.
4. WALDMANN, B. Rhinogenic origin of sympathetic ophthalmia (identity with spontaneous serous iritis). *Am. J. Ophth.*, 20: 618-625 (June) 1937.



# THE ADMINISTRATION OF VITAMIN B<sub>1</sub> BY INTRASPINAL INJECTION

## OBSERVATIONS AND DEDUCTIONS

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IN January, 1938 a United Press release appeared in the newspapers concerning a report read before the Pan-American Congress describing a new method of treating chronic neurologic disorders. The item was played up for news value and accorded the handling that most scientific or medical subjects receive when brought to the attention of the laity. For example, one metropolitan newspaper captioned the release with this headline: "Spine is Made Youth Fountain by Vitamin B<sub>1</sub>," and the item itself informed readers that "the value of the method (spinal injection) has been proved clinically in a large number of different types of nervous disorders, decided symptomatic improvement being noted in cases of hopeless cancer, beriberi, multiple sclerosis, alcoholic neuritis, sciatica, von Recklinghausen's disease, and infantile paralysis."

Physicians, particularly neurologists, who failed to read the release or who were in the habit of acquiring information concerning the latest advances in medicine from other sources than the newspaper were soon made aware of their shortcomings. Practically all patients whom we were treating for multiple sclerosis had read the release and urgently requested that they be given this highly promising treatment at once. In this fashion our attention was directed to the intraspinal injection of vitamin B<sub>1</sub> for the treatment of chronic neurologic disorders and we ultimately evaluated the treatment in a series of cases under our observation with results which will be described later. Our group of patients had the following

disorders: multiple sclerosis, poliomyelitis, encephalitis, and amyotrophic lateral sclerosis. All cases were chronic, and the majority were cases of multiple sclerosis. All patients receiving treatment were kept under observation for at least six months, and some for an even longer period of time.

Prior to our clinical evaluation of the administration of vitamin B<sub>1</sub> by intraspinal injection, the literature on vitamin B<sub>1</sub>, particularly that which pertained to its clinical use, was surveyed and reviewed. It is not the purpose of this report to attempt a complete description of vitamin B<sub>1</sub> based upon the review of the literature, nor even to review the literature on the application and the value of vitamin B<sub>1</sub> in neurologic disorders. However, certain facts which in our opinion seemed pertinent to the evaluation might warrant mention.

Vitamin B<sub>1</sub> seems to be concerned in two important processes of the living organism: (1) oxidation in the tissues, and (2) the breakdown and utilization of carbohydrates by the body. Both processes may be more properly classified as portions of the general metabolism. Peters and his associates have developed these concepts in their discussion of the basic role of vitamin B<sub>1</sub> in the human economy. Vitamin B<sub>1</sub> deficiency produced in the experimental animal or encountered in the beriberi patient is characterized by excessive amounts of pyruvic acid or the pyruvates in the blood. Peters, in describing a study of pigeons suffering from B<sub>1</sub> deficiency, apparently regards the impaired powers of the central nervous system of these birds to carry out normal oxidation of the carbohydrates as the "biochemical

lesion" of B<sub>1</sub> deficiency, and significantly mentions the accumulation of the pyruvates in the blood of his experimental fowl and of beriberi patients. The biochemical lesion can be abolished in vivo or in vitro by the addition of crystalline vitamin B<sub>1</sub>. Continuation of the deficiency in the experimental fowl is followed by convulsions of central nervous system origin. The condition of animals in experimental B<sub>1</sub> deficiency and that of patients suffering from beriberi (the manifestation of B<sub>1</sub> deficiency in human beings) are remarkably similar. Symptoms referable to impairment of the neural tissues are prominent features in both instances.

Beriberi, the condition caused by extreme or complete B<sub>1</sub> deficiency, is fortunately of rare occurrence in western countries. The question concerning the existence of B<sub>1</sub> deficiencies of less marked degree which could produce clinical manifestations is not so readily answered. The preponderance of evidence, however, indicates that subclinical B<sub>1</sub> deficiencies are not uncommon. The summary of the literature on vitamin B<sub>1</sub> by Wilder and Wilbur states that Cogwill estimates the daily B<sub>1</sub> requirement of the average adult to be about 300 international units; Harris and Leong estimate the daily requirement to be 250 to 500 international units. The summary continues that Baker and Wright reemphasize the fact that vitamin B<sub>1</sub> is not abundant in most foods. Fresh foods, on an average, contain about 1 international unit per gram, but the content varies considerably and is further diminished during the preparation and cooking of food for human consumption. Finally the vitamin content of the diet does not wholly enter the body, as much of it may be lost during the process of digestion and absorption of food in the alimentary tract.

It seems reasonable therefore to state that the fairly high daily requirements of vitamin B<sub>1</sub> and the factors of varying food content, destruction during preparation of food for human consumption, and loss of the dietary vitamin B<sub>1</sub> during digestion and

absorption, may work together to result in a higher incidence of mild to moderate B<sub>1</sub> deficiencies productive of clinical symptoms, than is commonly realized. The "biochemical lesion" of B<sub>1</sub> deficiency is majored in neural tissues, so many neurologic disorders, acute or chronic, might be due in part or entirely to B<sub>1</sub> deficiency.

The medical literature leaves no doubt but that vitamin B<sub>1</sub> is an important factor in certain nervous disorders and merits the title of "the antineuritic vitamin." Jolliffe, Colbert, and Joffe considered the relationship of diminished B<sub>1</sub> intake to neuritic symptoms to be definite. In their study of forty-two alcohol addicts, every alcoholic who developed polyneuritis had an inadequate vitamin B intake, while those whose intake was adequate did not develop polyneuritis. They believe "that alcohol has no direct toxic action on the peripheral nerves but that vitamin B<sub>1</sub> deficiency causes polyneuritis." Jolliffe and Colbert came to the same conclusions after a study of twenty-four alcohol addicts with polyneuritis. Seven patients on a borderline diet neither improved nor deteriorated. Eight patients on a moderate B<sub>1</sub> intake improved. Nine patients whose B<sub>1</sub> intake was approximately four times their estimated requirement improved rapidly and markedly. Two patients on the border diet responded quickly to the intravenous injection of crystalline B<sub>1</sub>. Theobald treated neuritic patients in the last trimester of pregnancy with dietary measures; the symptoms in four were completely relieved by the addition of B<sub>1</sub> to the diet. The fifth apparently suffered from other vitamin deficiencies, and required A and D medication in addition to B<sub>1</sub>.

Strauss and McDonald, on the basis of their experience with vitamin B<sub>1</sub> in four cases of polyneuritis of pregnancy, concluded that the prophylactic use of vitamin B<sub>1</sub> is indicated. Their first patient developed vomiting in the fourth month of pregnancy which increased in severity. After therapeutic termination of the pregnancy in the seventh month, a clear case of multiple

neuritis developed. The second patient also had multiple neuritis and vomiting of pregnancy. Miscarriage occurred and the patient grew steadily worse. Improvement followed the administration of iron and a diet rich in vitamins. The third patient had a typical polyneuritis of pregnancy with a macrocytic and hypochromic anemia. Improvement of the nervous disorder and of the blood occurred within ten days, and a healthy child was delivered at term. The mother was able to walk without difficulty shortly after the birth of the child.

Fouts, Gustafson, and Zervas report a critical case of vomiting of pregnancy in which polyneuritis developed. Vitamin B therapy was instituted, and the patient soon showed definite improvement. The parenteral administration of vitamin B<sub>1</sub> is recommended in all such cases as a prophylactic against the development of polyneuritis.

Vorhaus has pointed out that the neuritides most often seen are the sciatic, sacroiliac, and shoulder-girdle group. Such cases are frequently associated with focal infection and improvement has followed removal of tonsils, teeth, etc. However, cures are few in comparison with disappointments over the results of such procedures. Vorhaus uses vitamin B<sub>1</sub> in these conditions and observed marked improvement in a large number of cases even in the presence of a focus of infection.

There are many other informative reports describing the use of vitamin B<sub>1</sub> in the treatment of polyneuritis, but a sufficient number have been cited to demonstrate the results obtained from B<sub>1</sub> therapy in this disorder. The value of vitamin B<sub>1</sub> or the status of B<sub>1</sub> deficiency in other neuropathies is not so definite or well defined. Wexberg, however, after studying forty-seven patients suffering from cranial, spinal, or peripheral nerve disease, stated that in all such cases evidences of vitamin B<sub>1</sub> deficiency should be looked for. He found definite or strongly suggestive evidence of B<sub>1</sub> deficiency in all of his cases, and secured definite improvement from the use of vita-

min B<sub>1</sub> in patients with subacute combined degeneration of the cord, chronic progressive polyneuritis, and alcoholic polyneuritis.

Vorhaus, in an evaluation of B<sub>1</sub> therapy, stated that with the exception of beriberi, neuritis is the only clinical entity in which vitamin B<sub>1</sub> may be said to be of unquestionable value. Although studies of the relationship of vitamin B<sub>1</sub> and the susceptibility of experimental animals to herpes virus were inconclusive, Vorhaus used vitamin B<sub>1</sub> in postherpetic paresthesias and anesthetics and found that residual symptoms disappeared more quickly and that fewer patients had persistent anesthetics in the group receiving vitamin B<sub>1</sub> than in the untreated patients comprising the control group. Widenbauer reported vitamin B to be of value in the treatment of mild chorea and in a later paper described the use of vitamin B<sub>1</sub> by intramuscular injection in ten cases of spasmophilia. After one or two injections, the symptoms disappeared within twelve to seventy hours in eight of the ten cases.

Pfaffenberg and Mielke found that the cord symptoms in pernicious anemia were definitely relieved by large doses of vitamin B<sub>1</sub>. The vitamin therapy was supplementary to the usual anti-anemia measures. These investigators, however, call attention to the fact that the neurologic symptoms in pernicious anemia have not been proved to be caused by neural lesions referable to B<sub>1</sub> deficiency.

In all of the clinical studies mentioned thus far, vitamin B<sub>1</sub> was administered either orally, intramuscularly, or intravenously. In reviewing the literature, reference to the intraspinal administration of vitamin B<sub>1</sub> was discovered, but consideration of the report was deferred until complete information regarding the influence of vitamin B<sub>1</sub> had been obtained, regarding its rôle in the physiology of the body, the lesions produced by B<sub>1</sub> deficiency (particularly in nerve tissues), and the value of vitamin B<sub>1</sub> in at least some of the neuropathies (by oral, intramuscular, or intravenous therapy). The data on these points, as has been

reported, warranted investigation of the intraspinal administration of vitamin B<sub>1</sub>.

Friedeman apparently was the first to report the results obtained by the intraspinal administration of vitamin B<sub>1</sub>. Two patients suffering from marked Korsakow's syndrome, severe dementia, and complete paralysis, and one patient with cerebrospinal syphilis and complete paralysis of the musculature of the extremities and abdomen, were given intraspinal injections of vitamin B<sub>1</sub>. In all three cases, the patients regained muscular activity in about four months. Even the dementia improved so that the patients became completely oriented as to time and environment.

A dose of 500 international units of B<sub>1</sub> was given by epidural injection once a week. Later endolumbal injections were given. The time interval was gradually increased so that finally only one endolumbal injection was made in three weeks. The procedure was well tolerated. By-effects were observed only twice and consisted of nausea on the day of injection, and slight malaise and headache persisting for four days. In neither instance was it necessary to administer any drugs for relief.

Stern published a detailed study on the intraspinal administration of vitamin B<sub>1</sub>. The cases treated included inoperable cancer, ten; von Recklinghausen's disease, one; multiple sclerosis, two; degeneration of the pyramidal system of unknown etiology, one; thrombo-angiitis obliterans with pregangrenous condition of feet, one; duodenal ulcer with pulmonary tuberculosis, one; alcoholic neuritis of the supra-orbital nerve, one; neuritis of the sciatic nerve, one; cardiac decompensation with uremia and anuria, one; tabes dorsalis, one; hypertrophic spondylitis, two; osteoporosis of the spine, one; Paget's disease, one; intractable pruritus ani and vulvae, two; beriberi, one; and acute poliomyelitis, one.

The warranty for the intraspinal administration of vitamin B<sub>1</sub> according to Stern is that "avitaminotic nerve fibers seem to have an urgent hunger for this

vitamin . . . which acts as a catalytic agent and which is essential for carbohydrate metabolism . . . after intravenous injection, the vitamin appears to be quickly eliminated in the urine, while after intraspinal injection, the elimination is found to be spread over a longer period of time." From his observations in these twenty-eight cases, Stern concluded that "many chronic or incurable conditions of the central and peripheral nervous system may respond favorably to the intraspinal subarachnoid injection of synthetic vitamin B<sub>1</sub>. It should prove of particular value in cases of multiple sclerosis, encephalitis, syphilis and poliomyelitis."

Retarded elimination of vitamin B<sub>1</sub> would obviously be advantageous, as it would remain available for use by the nerve cells over an extended period of time. It has been shown that following oral, intramuscular, or intravenous administration, vitamin B<sub>1</sub> is so rapidly eliminated that correction of a pronounced deficiency requires many doses at frequent intervals.

Stern's favorable conclusions from his observations in the series of twenty-eight cases would indicate that the intraspinal administration of vitamin B<sub>1</sub> offers, among other advantages, retarded elimination. We were unable, however, to locate data that, in our opinion, demonstrated sufficient retardation of elimination as to be responsible for any material change in the clinical results. We were also unable to find information in the details regarding the patients' responses to treatment which enabled us to regard the therapy as being of value. Improvement in many of the cases could, in our opinion, be as well ascribed to other factors as to the intraspinal injections of vitamin B<sub>1</sub>. For example, the marked improvement observed in the two cases of multiple sclerosis after four and five injections respectively could have been due to spontaneous temporary remissions which are known characteristically to occur in multiple sclerosis, or to psychic response (suggestion) on the part of the patient without organic improvement.

CHART I

Case	Sex	Age	History	Diagnosis	Treatment	Reaction	Result
1	F	55	First exam. 11/13/37. Onset 2 yrs. previous, pain in knees on walking. Unsteady on feet, and stiffness of legs. Urgency and incontinence.	Multiple sclerosis	6/1/38 10 mg. 6/8/38 10 mg. 6/15/38 30 mg. (intraspinaly)	Severe headache after each treatment and more walking difficulty after last one; refused further injections.	Unimproved (subjectively worse).
2	F	14	First exam. 8/27/36. Spastic, dragging gait, extreme stiffness of legs. Typical neurologic findings.	Multiple sclerosis	3/30/38 10 mg. 4/13/38 30 mg. 4/20/38 30 mg. 5/4/38 30 mg. 5/11/38 30 mg. 5/25/38 30 mg. (intraspinaly)	Severe headaches and felt weaker after each treatment. After a 2 wk. interval refused to continue after 6 injections.	Unimproved (must have support in walking).
3	M	35	First exam. 2/18/38. Onset 1½ yrs. previous with stiffness in left ankle growing steadily worse. Now had stiffness of both legs, and knees ache. Continuous fibrillary twitching of shoulder, girdle and pectoral muscles. Grew progressively worse during 3 months under treatment and had to discontinue.	Amyotrophic lateral sclerosis	3/23/38 10 mg. 3/30/38 30 mg. 4/6/38 30 mg. 5/4/38 30 mg. 5/11/38 30 mg. 5/18/38 30 mg. 6/11/38 30 mg. (intraspinaly)	Unable to lift legs at all after some treatments, severe headaches after some. Discomfort so severe refused to come for treatment between third and fourth injections and on another occasion refused to come for 2 weeks.	Became progressively weaker—complete paralysis of extremities with incontinence (8/16/38).
4	F	54	First exam. 3/9/36. Onset one year previous with pain in legs and weakness in left leg and some loss of sensation of arms and hips, and tendency to give out when walking. Right foot dragged in walking. Numbness over right hip. Frequent backaches. Neurologic findings positive.	Multiple sclerosis	10 mg. daily from 3/9/38 to 6/10/38, then 3 times per week for 2 months, then every third day for one month. (intramuscularly)	None	Became progressively weaker (lost 5 lbs. during treatment).
5	F	35	First exam. 6/14/38. Pain and numbness in knees for 1 yr., worse past month. Could not walk straight, or manage feet right. Weak.	Multiple sclerosis	7/6/38 10 mg. 7/13/38 20 mg. 7/20/38 30 mg. 7/27/38 30 mg. 8/3/38 30 mg. 8/10/38 30 mg. 8/16/38 30 mg. 8/24/38 30 mg. 9/7/38 30 mg. 9/14/38 30 mg. 9/21/38 30 mg. 9/28/38 30 mg. 10/12/38 30 mg. 10/19/38 30 mg. (intraspinaly)	Grew progressively weaker, with temporary minor remissions—in spite of taking the injections religiously every week. Refused to let herself complain of any discomfort, hoping for a cure.	Unimproved (unable to walk without support).

CHART I (Continued)

Case	Sex	Age	History	Diagnosis	Treatment	Reaction	Result
6	F	6	Born with bilateral clubfeet. Supernumerary right little toe. Only a trace of power in either calf and little in hamstrings. Extensors of hands and feet powerless.	Spina bifida or chronic polio-myelitis	1 mg. daily for 7 weeks—then 2 mg. daily for 7 weeks. (intramuscularly)	None	Grew worse (atrophy increased).
7	M	7	Onset at 2 yrs.—weakness of back with difficulty in getting up from prone position. Marked hypertrophy of calves of legs. In March 1938 was unable to walk. Entirely helpless and developing contractures.	Progressive muscular dystrophy	2 mg. daily from 3/7/38 to 6/27/38. (intramuscularly)	None	Unimproved.
8	M	57	Claimed onset was sudden following a fright 4 months before. Pain in left leg first, with later spasticity and then weakness in legs and difficulty in walking. Very suggestible individual. Neurologic findings positive.	Multiple sclerosis	3/30/38 10 mg. 4/6/38 30 mg. 4/13/38 30 mg. 4/20/38 30 mg. 4/27/38 30 mg. 5/4/38 30 mg. 5/11/38 30 mg. 6/1/38 30 mg. (intraspinaly)	Some headache after treatment and feet weaker for 2 days after each one.	Improvement in walking. Decrease in spasticity of legs. (Remission?)
9	M	36	Onset 3 years previous general weakness, particularly in legs, staggering gait for past year. Tired from waist down, loses balance on turning quickly. A most coöperative patient in completing all treatment no matter how unpleasant. Neurologic findings positive.	Multiple sclerosis	10 mg intramuscularly daily 2/25/38 to 4/13/38 then: 4/13/38 10 mg. 4/20/38 20 mg. 4/27/38 30 mg. 5/4/38 30 mg. 5/11/38 30 mg. 6/1/38 10 mg. 6/8/38 10 mg. 6/15/38 10 mg. 6/22/38 10 mg. 7/6/38 10 mg. 7/13/38 10 mg. 7/20/38 10 mg. 7/27/38 10 mg. 8/3/38 10 mg. 8/10/38 10 mg. 8/16/38 10 mg. 8/24/38 10 mg. 9/7/38 10 mg. 9/14/38 10 mg. (intraspinaly) 7/2/38 10 mg. 7/28/38 10 mg. (intraspinaly)	Insomnia and throbbing pains in back followed all treatments of 30 mg. dosage, but 10 mg. did not cause discomfort.	Although anxious to be helped showed no sustained improvement after 48 daily intramuscular injections followed by 4½ months of weekly intraspinal injections. Legs twitch and pound in walking.
10	F	46	Onset 11 years previous after childbirth, with difficulty	Multiple sclerosis		Terrible headache with vomiting and sweating	Unimproved. Refused to take further treat-



CHART I (Continued)

Case	Sex	Age	History	Diagnosis	Treatment	Reaction	Result
			in walking. Slowly getting worse. Unable to walk unassisted (6/27/38). Legs spastic. Other neurologic findings positive.			followed second intraspinal treatment. Symptoms persisted 5 days, followed by 3 weeks of prostration.	ments.
11	F	27	Onset 8 years before with gradually progressing pain and weakness of lower back followed by generalized body weakness and ataxia. Also emotional upsets, intention tremor of hands, urinary incontinence, diplopia and nystagmus, spastic, drags right leg, falls spontaneously. Neurologic signs positive.	Multiple sclerosis	3/23/38 10 mg. 3/30/38 30 mg. 4/6/38 10 mg. 4/13/38 30 mg. 4/20/38 30 mg. 5/11/38 30 mg. 6/8/38 30 mg. (intraspinally)	No reaction to 10 mg. but 30 mg. did cause persistent vomiting, headaches. Had to remain in bed. Because of such reactions long periods intervened between injections.	Grew progressively worse. Fell off chair, fractured thumb during third month of treatment. Now confined to bed, incontinent.
12	F	..	Onset 10 years before, gradually progressive spastic paralysis of legs. Now constantly spastic in extreme degree—bedridden.	Multiple sclerosis	Received 10 mg. on 2 occasions (one week interval). (intraspinally)	Severe reaction after each injection. Refused further treatments.	No improvement.
13	F	16	Condition present since birth. Markedly tremulous speech. Legs and arms extremely spastic, very unstable, wide-based gait. Makes grimaces spontaneously. Foot drop bilaterally with spontaneous right Babinski, and pains in legs for last year. Generalized body tremors exaggerated in Romberg test.	Spastic quadriplegia	5/13/38 to 6/15/38 given 10 mg. daily for one month. (intramuscularly)	None	No improvement.
14	M	38	Onset followed "grippe" in 1933. Partial numbness of both forearms with gradually increasing weakness of both, with tremor and hypertonicity. Masked fascies. Propulsive gait.	Post-encephalitic syndrome	3/23/38 10 mg. 3/30/38 30 mg. 4/6/38 30 mg. 4/27/38 30 mg. 5/4/38 30 mg. 5/11/38 30 mg. 6/1/38 30 mg. 6/8/38 30 mg. 6/15/38 30 mg. 6/22/38 30 mg. (intramuscularly)	None (Patient a stoic)	Growing worse. In third month felt right arm weaker. In fourth month cramps in arm. After seven months difficulty in drinking or moving lips.
15	M	47	Gradually progressive weakness of right upper extremity for 2 years. Shooting	Amyotrophic Lateral Sclerosis	10 mg. daily for nine weeks beginning 3/4/39. (intramuscularly)	None	No improvement. Fingers more painful. Pain in neck developed.

CHART I (Continued)

Case	Sex	Age	History	Diagnosis	Treatment	Reaction	Result
16	M	35	pains, and pins and needles sensation in same member. Atrophy of muscles of interossei and lumbricales (right). Similar complaints to less extent in left upper extremity. Atrophy of both deltoids. Fibrillary twitchings in the pectoralis, biceps and triceps. Walks with wide base. Bedridden spastic paralysis (quadriplegia) with incontinence. Duration 7 years. Marked speech and general bodily tremor, gradually progressive loss of sensation in hands. All neurologic signs positive.	Multiple sclerosis	3/8/38 to 3/18/38 10 mg. daily intravenously and 10 mg. intramuscularly. Then: 10 mg. intramuscularly daily for 7 weeks. Then 10 mg. first dose and thereafter 30 mg. intraspinally for 3 months.	Very coöperative. Minimized his discomfort but had one or two uncomfortable days after each intra-spinal treatment.	Spontaneous muscle twitchings frequent.  No improvement. Remains bedridden. Incontinence more frequent.
17	M	32	Onset gradual beginning 8 years before with facial palsy (right). Later diplopia. Weakness in legs with spasticity past 3 years, unable to get up and down stairs. Slow, deliberate speech. Tremors of legs (coarse) in walking. Feeling of generalized trembling. Neurologic signs positive.	Multiple sclerosis	1/31/38 to 2/10/38 10 mg. daily intravenously 10 mg. intramuscularly. 2/10/38 to 3/31/38 10 mg. intravenously daily. 3/31/38 to 6/8/38 30 mg. intraspinally at 5 day intervals (first dose 10 mg.).	Very coöperative. Minimized discomfort, but had repeated reactions of severe back pain following injections.	No improvement. Distinctly worse a year after starting treatment.
18	F	27	Gradually progressive weakness in lower extremities. Duration 8 years. Numbness after sitting, difficulty climbing stairs, occasional leg twitching. Neurologic signs positive.	Multiple sclerosis	10 mg. daily for 6 weeks begun 3/8/38. (intramuscularly)	None	No improvement.
19	M	29	Tremor in right arm developed 8 years after auto accident. Poliomyelitis 1½ years before, leaving weakness and atrophy of left hand, arm	Poliomyelitis Residual Paralysis (Possible encephalomyelitis)	10 mg. first dose and then 30 mg. weekly for 6 weeks. (intraspinally)	Severe headaches for 2 days—had to remain away from his work.	No improvement.

CHART I (Continued)

Case	Sex	Age	History	Diagnosis	Treatment	Reaction	Result
20	F	36	and shoulder, constant tremor of right hand persists. Generalized pains like "toothache" particularly in hands and legs developed in April 1938, with some numbness. On April 21, neurologic exam. showed: bilateral foot drop, absent knee and ankle jerks complete loss of motor power (both legs) glove and stocking anesthesia, tremor and weakness both hands, positive Romberg. Ptosis right. History of excessive indulgence in alcohol.	Alcoholic polyneuritis	10 mg. b.i.d. intramuscularly for 6 weeks, then daily for 6 weeks. Subsequently 5 mg. orally b.i.d.	None	Numbness decreased in 10 days and disappeared in 20 days. Able to walk with help after 7 weeks and alone after 10 weeks. Jan. 1939—is attending dancing school weekly.

In view of the rôle of vitamin B<sub>1</sub> in the metabolism in the nerve tissues, the improvement which follows its use in the neuritides, the frequent occurrence of B<sub>1</sub> hypovitaminosis in many of the neuropathies, the nature of the nervous symptoms occurring in beriberi, and the favorable opinions of the investigators who had used and reported the intraspinal injection of vitamin B<sub>1</sub>, we arranged for clinical evaluation of this procedure with the hope of confirming its value in the degenerative neurological disorders. The investigation was conducted in the Neurological Clinic of the New Jersey Orthopedic Hospital (Orange, New Jersey). Various types of organic disorders are seen in this Clinic which accepts patients from the northern half of the State. Vitamin B<sub>1</sub>\* was administered by intraspinal subarachnoid injections. The dose, the time interval between doses, and the duration of treatment are shown in Chart I. The table also includes

data regarding the sex, the age, a digest of the pertinent facts of the history pertaining to the neurologic disorder, reactions (by-effects) caused by the treatment, and the results. It was planned to administer vitamin B<sub>1</sub> orally, intramuscularly, and finally intraspinally, interrupting the therapy at any point if improvement was such that further treatment seemed unnecessary. The patients were easily interested in the treatment. Although most of them had tried many different remedies without improvement during a period of months or years, they had developed a "grasping for a straw" philosophy, and were willing to try anything which offered hope. The complete progressive course of therapy could not always be applied in every case as is evident from inspection of the table. The reasons will be discussed later.

A series of twenty patients was started on the course of therapy which was planned to include the oral, intramuscular, and intraspinal administration of vitamin B<sub>1</sub> in each case. The following conditions were treated: multiple sclerosis, twelve; amyotrophic lateral sclerosis, one; postencephali-

\* Acknowledgment is made of the courtesy of Hoffmann-La Roche, Inc., Nutley, New Jersey who provided generous supplies of berocca (synthetic vitamin B<sub>1</sub>) for use in this study.

tic syndrome, one; spastic quadriplegia, one; poliomyelitis, one; progressive muscular dystrophy, one; spina bifida (or chronic poliomyelitis), one; and alcoholic polyneuritis, one. Complete recovery was obtained in only one case—the case of alcoholic polyneuritis. Three of the twelve patients with multiple sclerosis refused to continue treatment on account of the pain and discomfort caused by the intraspinal injections of vitamin B<sub>1</sub>; no improvement was observed in these patients from the beginning of treatment to the time when they discontinued treatment. Seven of the patients with multiple sclerosis who continued with the treatment as long as requested failed to secure sustained improvement. Two of the patients with multiple sclerosis, having been treated with intramuscular injections of vitamin B<sub>1</sub> for a period of two to four months without improvement, were not given the intraspinal injections. Our observation of the seven patients who had received the injections without improvement made us reluctant to subject the patients to the discomfort, particularly since the intramuscular injections had effected no improvement.

In the remaining seven cases of various neurologic disorders, intensive vitamin B<sub>1</sub> therapy, administered intramuscularly or intraspinally, was not followed by sustained improvement.

Other investigators may be able to confirm the findings of Friedeman and Stern that the intraspinal injection of vitamin B<sub>1</sub> in chronic neurologic disorders brings about improvement. In our series of cases the procedure proved of no value. Deficiency of vitamin B<sub>1</sub> may also be shown in the future to be a factor, or even the basic cause, of multiple sclerosis or other degenerative neurologic disorders. Our results, however, indicate that if the nerve degeneration has reached the stage of irreversible change, return of motor or sensory function will not occur even though massive doses of vitamin B<sub>1</sub> are injected intraspinally over a long period of time. Considering the number of patients in our group and the

youth of many of them, it would seem that there would be some in whom nerve degeneration had not reached the stage of irreversible change. In these cases (if vitamin B<sub>1</sub> deficiency caused the disorder) definite and sustained improvement such as return of function in a partially paralyzed arm or leg, should have occurred.

In the one case of multiple sclerosis in which improvement occurred, a number of factors have to be considered in evaluating this response. The patient, formerly a hardy and robust man, was most anxious to improve and therefore was extremely suggestible. The improvement, including the neurologic signs, was still apparent two months after conclusion of the intraspinal injections. After the passage of another two months, however, he went to another clinic where his condition was again diagnosed as a very evident case of multiple sclerosis. In our opinion, the improvement was probably due to a spontaneous and temporary remission, entirely unrelated to the intraspinal injections of vitamin B<sub>1</sub>.

The intramuscular injections of vitamin B<sub>1</sub> caused no discomfort other than the pain usually experienced in any intramuscular injection from insertion of the needle. This part of the treatment, as well as the oral treatment, therefore, was not disturbing to the patients. The intraspinal injections, however, were painful even though a local anesthetic was used, and very frequently reactions such as headache or vomiting developed afterward and lasted as long as two days. Some patients refused to even start the treatment when these facts were made known to them by their fellow patients. Other patients, although they started treatment enthusiastically, could not be persuaded to continue treatment after experiencing one or two reactions. This was the experience with six of our patients.

Goodhart and Jolliffe, and Wechsler have established beyond question the fact that function can and frequently does return in paralytic conditions caused by a true vitamin B<sub>1</sub> deficiency. This response was

observed in the last case listed in the accompanying table. The patient, a 36 year old woman, had a typical case of so-called alcoholic polyneuritis (which in the future may be more properly named avitaminotic polyneuritis). Although a bed-ridden invalid previous to treatment, she recovered normal function of her paralyzed arms and legs and complete return of sensory function after less than three months of vitamin B<sub>1</sub> therapy administered intramuscularly. She is now healthy, normally ambulatory, and, according to most recent reports, taking dancing lessons regularly.

Due to the observations of McCormick, we included the case of poliomyelitic residual paralysis in our series. McCormick pointed out the similarities between poliomyelitis and beriberi and posed the question whether the susceptibility of children to poliomyelitis was related to decreased reserves of vitamin B<sub>1</sub> caused by increased physical activity in the summer months. If decreased vitamin B<sub>1</sub> reserves are responsible, this neatly explains both the greater severity and the higher incidence of the disease during the summer. While there is insistence upon an adequate intake of vitamins A, C, and D in the growing child, the concomitant need for vitamin B<sub>1</sub> is left in the background. The relatively recent synthesis of vitamin B<sub>1</sub> has made it readily available for therapeutic use and refocused attention on its possible rôle in the resistance to poliomyelitis.

The disability in our patient was of one and one-half years' duration and therefore irreversible changes probably had occurred in the neural tissues. Other than the residual symptoms, the patient's condition was excellent. As was expected, the intraspinal injection of vitamin B<sub>1</sub> over a period of weeks failed to bring about improvement. Notwithstanding the results in this case, further intensive study of vitamin B<sub>1</sub> therapy in poliomyelitis seems warranted. Presumably, the vitamin should be administered intravenously or intramuscularly, immediately after the condition has been diagnosed.

## SUMMARY

The widespread publicity given by the daily press to the inaccurate, optimistic accounts of medical research frequently arouses false hopes in those afflicted with the disorders which happen to be the subjects of the scientific investigation unfortunately exploited for sensational news value. Our attention was directed to the intraspinal injection of vitamin B<sub>1</sub> in the treatment of chronic neurologic disorders by patients who had such disorders and who had learned of the injections through the accounts in their newspapers. A survey of the medical and scientific literature indicated that there was a relationship between vitamin B<sub>1</sub> and metabolism in the neural tissues, that a "biochemical lesion" in the central nervous system was caused by B<sub>1</sub> hypovitaminosis, that the clinical manifestations of beriberi (absolute B<sub>1</sub> hypovitaminosis) included nervous symptoms now acknowledged to be remarkably similar to those seen in degenerative neurologic disorders, and that the use of vitamin B<sub>1</sub> in some disorders of the peripheral nerves, for example the neuritides, brings about improvement. The intraspinal injection of vitamin B<sub>1</sub>, in the light of the survey, seemed to merit consideration, particularly since reports of improvement following such therapy appeared in the medical literature. The administration of vitamin B<sub>1</sub> by intraspinal injections (and other avenues as well) was evaluated in a group of patients suffering from chronic neurologic disorders. Our experience with this type of therapy has led to several conclusions.

## CONCLUSIONS

1. Intraspinal injections of vitamin B<sub>1</sub> in a series of nineteen cases of chronic degenerative neurologic disorders and one case of alcoholic polyneuritis failed to bring about sustained improvement in the chronic degenerative disorders. The alcoholic polyneuritis apparently was cured by intramuscular injections of vitamin B<sub>1</sub>; this

condition is recognized to be due to B<sub>1</sub> hypovitaminosis.

2. The intraspinal injections were very frequently followed by such severe reactions that a substantial number of even the most enthusiastic and hopeful patients discontinued treatment. Since the injections, in our experience, are valueless, discontinuation of treatment was a matter of no concern, except for the disappointment and the needless discomfort.

3. The lack of improvement indicates that B<sub>1</sub> hypovitaminosis is not the basic cause of the degenerative disorders and probably not even an important factor in their development or rate of progress.

4. The value of vitamin B<sub>1</sub> in some of the disorders of the peripheral nerves, for example the neuritides, suggests that it may prove of value in only those conditions in which nerve degeneration has not reached the stage of irreversible change. On this premise, treatment of poliomyelitis in its earlier stages with vitamin B<sub>1</sub> warrants further investigation. Poliomyelitis in the later stages or residual symptoms following an acute attack of poliomyelitis will probably not be improved by treatment with vitamin B<sub>1</sub>.

5. Newspaper publicity of medical research, particularly in the field of therapeutics, is deplored. False hopes are aroused in patients who insist upon prolonged and frequently painful treatment of dubious or unproved value. The discontent and disappointment caused by failure of the treatment are a menace to the patient's general welfare.

#### REFERENCES

PETERS, RADIN, and THOMPSON: Brain respiration. A chain of reactions as revealed by experiments upon

catatorulin effect. *Biochem. J.*, 29: 53, 1935. The relation of pyruvic acid in brain to certain tissue poisons. *Biochem. J.*, 29: 63, 1935.

PETERS. The biochemical lesion in vitamin B<sub>1</sub> deficiency. *Lancet*, 1: 1161, 1936.

WILDER and WILBUR: Diseases of metabolism and nutrition. Review of certain recent contributions. *Arch. Int. Med.*, 59: 512, 1937.

HARRIS and LEONG. The excretion of vitamin B<sub>1</sub> in human urine and its dependence on the dietary intake. *Lancet*, 1: 886, 1936.

BAKER and WRIGHT. The vitamin B<sub>1</sub> content of foods. *Biochem. J.*, 29: 1802, 1935.

JOLLIFFE, COLBERT, and JOFFE. Observations on the etiologic relationship of vitamin B (B<sub>1</sub>) to polyneuritis in the alcohol addict. *Am. J. M. Sc.*, 191: 515, 1936.

JOLLIFFE and COLBERT. The etiology of polyneuritis in the alcohol addict. *J. A. M. A.*, 107: 642, 1936.

THEOBALD. Neuritis in pregnancy successfully treated with vitamin B<sub>1</sub>. *Lancet*, 1: 834, 1936.

STRAUSS and McDONALD. Polyneuritis of pregnancy. *J. A. M. A.*, 200: 1320, 1933.

FOUTS, GUSTAFSON, and ZERFAS. Successful treatment of a case of polyneuritis of pregnancy. *Am. J. Obst. & Gynec.*, 28: 902, 1934.

VORHAUS. The present evaluation of vitamin B<sub>1</sub> therapy. *Am. J. Diges. Dis. & Nutrition*, 3: 915, 1937.

WEXBERG. Diseases of the nervous system caused by nutritional deficiency. *South. M. J.*, 30: 334, 1937.

WIDENBAUER. Die Behandlung der Spasmophile mit krystallisiertem Vitamin B<sub>1</sub>. *Monatschr. f. Kinderh.*, 70: 82, 1937.

PFÄFFENBERG and MIELKE. Zur Vitaminbehandlung funikulärer Spinalerkrankungen. *Klin. Wchnschr.*, 16: 919, 1937.

FRIEDEMANN. Epidural and endolumbal administration of vitamin B<sub>1</sub>. *Schweiz. Arch. f. Neurol. u. Psychiat.*, Suppl., 39: 236, 1937.

STERN. The intraspinal (subarachnoid) injection of vitamin B<sub>1</sub> for the relief of intractable pain, and for the inflammatory and degenerative diseases of the central nervous system. Preliminary report. *Am. J. Surg.*, 39: 495, 1938.

STERN. Intraspinal (subarachnoid) injection of vitamins B<sub>1</sub> and C in acute poliomyelitis. *Clin. Med. & Surg.*, 45: 108, 1938.

GOODHART and JOLLIFFE. Effects of vitamin B (B<sub>1</sub>) therapy on the polyneuritis of alcohol addicts. *J. A. M. A.*, 110: 414, 1938.

WECHSLER. Multiple peripheral neuropathy versus multiple neuritis. *J. A. M. A.*, 110: 1910, 1938.

McCORMICK. Poliomyelitis: vitamin B deficiency a possible factor in susceptibility. *Canad. M. A. J.*, 38: 260, 1938.



# NERVE BLOCK ANESTHESIA FOR FOOT SURGERY

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THERE sometimes arises an occasion when some type of surgical procedure must be done on a foot and the condition of the patient will not permit the use of a general nor a spinal anesthetic and local infiltration will not suffice for the work to be done.

Such an occasion presented itself two years ago in a patient of mine. He had a compound lateral dislocation of the ankle joint, fracture of the medial malleolus, lateral malleolus and fracture of the neck of the astragalus. Due to the lateral position of the foot a very marked tension was placed on the posterior tibial nerve and artery so that the foot had to be reduced very soon to prevent gangrene from occurring. General or spinal anesthesia was out of the question due to a severe head injury and shock. The patient was semi-conscious and an anesthetic was necessary. Local infiltration obviously was insufficient for the magnitude of the work to be done.

A nerve block anesthetic was then administered according to the technique described below. The patient soon quieted down, his muscles relaxed and the reduction of the dislocation and fractures was easily accomplished. This same type of block anesthesia has since been done on eleven patients and the anesthesia has proved excellent in all. The operations for which this anesthetic was used include: five bunion operations; one triple stabilization (old man with fractured os calcis of long duration); one tendon suture; two infected plantar space abscesses; one removal of osteochondroma from metatarsal; one fresh os calcis fracture (Böhler reduction).

*Anatomic Considerations.* There are only two main nerves that supply sensation to the leg and foot. These are the tibial and saphenous branch of the femoral. The

saphenous is purely cutaneous in its distribution and supplies a narrow area over the anteromedial aspect of the leg for about half the distance from the knee to the ankle. It would be hard to block with novocaine because of some variation in its position as it comes down out of the thigh. The tibial nerve divides into the posterior tibial and the common peroneal. The tibial and common peroneal have a very definite and unvarying location and can be easily found and injected. Both posterior tibial and common peroneal give off muscular, articular and sensory branches and these branches supply all of the muscles of the leg and foot and all of the sensation to the leg and foot except that small area supplied by the saphenous branch of the femoral.

If the tibial and common peroneal nerves were completely blocked with novocaine an anesthesia of muscles and skin should be present in the foot and in most of the leg. Because of the saphenous nerve distribution, surgery on the leg itself would not be possible, but surgery on the foot should be definitely possible.

*Technique of Administration.* The patient should first be placed on the operating table on his stomach. The knee is flexed, the flexion crease located, and the skin prepared. A needle is inserted into the skin in the flexion crease behind the knee at a point just a little to the outside or lateral to the center of the leg. The tibial nerve lies not exactly in the midline, but a very slight distance to the lateral side of the middle. Five c.c. of 2 per cent novocaine is injected just beneath the skin at this site. At this injection the needle point lies just beneath the skin, not in the skin and not penetrating the deep fascia. The medial cutaneous branch of the tibial often comes off higher than the other cutaneous or muscular

branches and comes down the leg more superficial to but parallel to the tibial and posterior tibial nerves. This injection, therefore, when placed in the subcutaneous tissue at this site, will block sensation coming through the medial cutaneous branch of the tibial.

The needle is inserted deeper without changing its location. Just after piercing the deep or popliteal fascia, the tip of the needle will be on or immediately adjacent to the tibial nerve. Fifteen c.c. of 2 per cent novocaine is injected here. It is not necessary to try to place the novocaine directly into the nerve trunk. If it merely surrounds the nerve it will be absorbed sufficiently to produce anesthesia, although if it can be injected directly into the nerve it will probably be a better and quicker anesthetic.

The common peroneal nerve has a constant, unvarying location as it curves downward around the head and neck of the fibula. A needle is inserted on the lateral or posterolateral aspect of the fibula just below the prominence of the head of the fibula. Most often when this is done the patient will feel a sharp electric shock run down the leg. Ten c.c. of 2 per cent novocaine is injected here.

The patient is turned over and the foot prepared for operation. Within ten minutes the foot is well anesthetized and the leg muscles relaxed.

#### DISCUSSION

There are very few contraindications. Some patients may be hypersensitive to novocaine, but I have never seen any unusual or bad reactions. Infections of the bone or skin or soft tissue at the site of injections should constitute a contraindication. Most patients will complain of feeling slightly dizzy for about fifteen minutes following the injection of this much novocaine, but the reaction always passes off within twenty minutes. The duration of the anesthetic is from thirty minutes to an hour. Sensation and muscle return have always been normal within two hours after the anesthetic is given and no bad results have ever been noted from its use.

This particular nerve block as presented here is not mentioned in available articles or texts on local or regional anesthesia, but

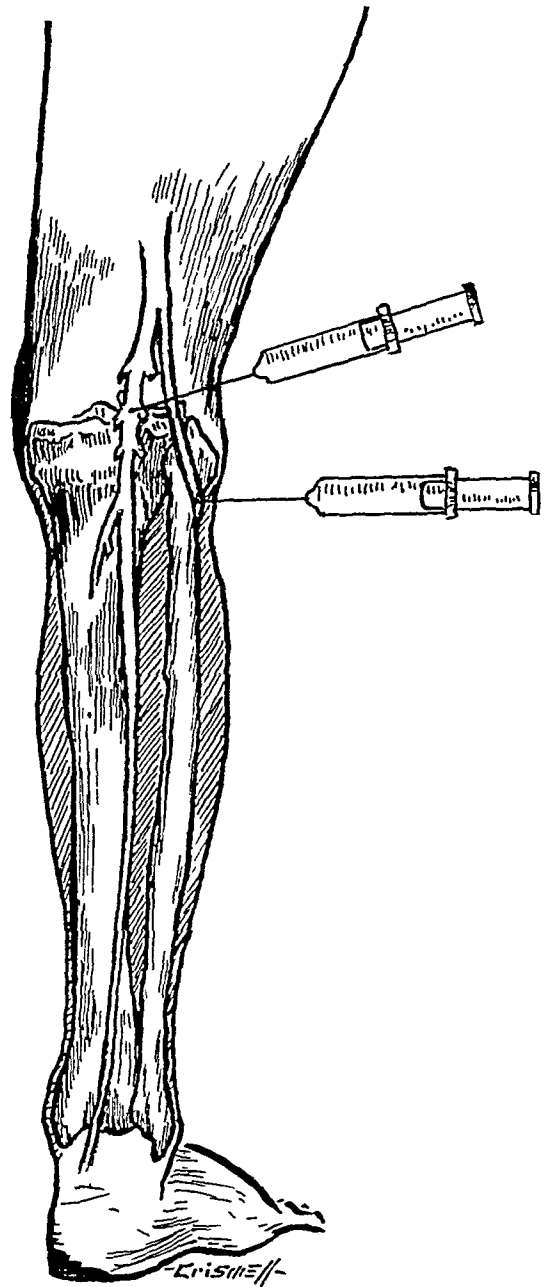


FIG. 1. Sites of injection.

because of its simplicity and ease of administration seems to have a definite field of usefulness in certain types of patients who cannot or who prefer not to have a general or spinal anesthetic.

#### SUMMARY

A new regional nerve block anesthesia is presented that is satisfactory in foot surgery



# A METHOD FOR THE CONTROL OF POSTOPERATIVE PAIN IN HALLUX VALGUS OPERATIONS\*

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ONE of the annoying after-effects of the operation for hallux valgus is the pain, which may persist for five to six weeks. It is reasonable to expect a slow and rather painful convalescence since the operation is essentially an arthroplasty. To obviate the postoperative pain, it seemed worthwhile to crush the sensory branches innervating the region and thus produce a temporary anesthesia. This would not only add to the comfort of the convalescence, but would permit motion of the joint much earlier than is usually the case.

Since crushing of the nerve without ligature or section will allow reestablishment of normal sensation within a reasonable period of time, there is no contraindication to this procedure providing due care is taken to avoid pressure on the anesthetized area during the first eight weeks. At the end of this time normal sensation is fully reestablished.

*Anatomy.* The medial aspect of the metatarsophalangeal joint is innervated by a dorsal twig derived from a branch of the superficial peroneal nerve which anastomoses with one from the saphenous nerve. The lateral aspect of the joint receives its sensation through a trunk derived from the anastomosis of the medial dorsal cutaneous nerve to the great toe with one from the deep peroneal nerve to the first interosseous space. These nerves to the joint are readily exposed just proximal to the latter on either side.

*Operative Technique.* After anesthetization with  $\frac{1}{2}$  per cent novocaine and adrenalin, the joint is exposed by a curved dorsomedial incision. The superficial layers

are dissected backward and laterally. The medial and lateral dorsal digital nerves are isolated and crushed for a distance of 1 cm. with a hemostat. Care is necessary not to sever them.

The technique for the reconstruction of the joint consists principally of chiseling off the greater part of the first metatarsal head, reshaping the new head, and interposing between the joint surfaces a long flap of capsule, the base of which is attached to the metatarsal bone. The wound is closed and the toe is then placed in a splint and strongly abducted by a pad between the first and second digits.

TABLE I

Case	Age	Ex- trem- ity	Pain	Return of Sen- sation, Weeks	Active Motion Insti- tuted	Days in Hos- pital
I	46	Right	Absent	8	1 week	4
II	62	Right	Absent	7	5 days	4
III	52	Right	Absent	8	1 week	3
		Left	Absent	8	1 week	
IV	38	Right	Absent	8	1 week	4
		Left	Absent	8	1 week	
V	45	Right	Absent	9	10 days	4
		Left	Absent	9		
VI	46	Right	Absent	8	1 week	5
		Left	Absent	8	1 week	
VII	42	Right	Absent	7	1 week	5
		Left	Absent	7	1 week	
VIII	47	Right	Absent	9	1 week	7
		Left	Absent	9	1 week	
IX	44	Right	Absent	8	1 week	7
		Left	Absent	8	1 week	

*Results.* In nine patients a total of sixteen operations was done by the method described. (Table I.)

\* From the Orthopedic Department, Carney Hospital, Boston, Mass.

In all cases pain was absent throughout the entire convalescence and motion was possible much earlier than usual. Sensation returned within seven to nine weeks.

A roomy walking shoe with a straight last, wide toe and wide shank should be carefully fitted. It is of the utmost importance in the after-care to emphasize to the patient that wide shoes must be worn until sensation returns because of the danger of pressure sores.

#### CONCLUSIONS

1. A method which minimizes the pain after operation for hallux valgus is described.
2. Motion is instituted much earlier than usual.
3. The period of disability is definitely shortened.
4. This method may obviate the occurrence of hallux rigidus.



THE terms spontaneous and pathological fracture are sometimes used as synonyms. It is an advantage to distinguish two groups of fractures in which the traumatic factor is unimportant: (a) spontaneous fractures where the bone is normal, and (b) pathological fractures where there is a pathological abnormality of the bone.

From—"Fractures and Other Bone and Joint Injuries" by R. Watson-Jones (Williams and Wilkins).

# OSTEITIS DEFORMANS (PAGET'S DISEASE OF BONES)\*

## A REVIEW OF FIFTY-ONE CASES

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APPARENTLY as old as man himself yet comparatively new as a recognized clinical entity, osteitis deformans can no longer be considered a rare condition. The Neanderthal man has been suggested as a not unlikely example; it has been described in Egyptian mummies and in both its generalized and monostotic varieties in the rather recently uncovered remains of prehistoric American Indians. Moreover, pathologically similar lesions have been described in fowl, horses, and goats, and fairly typical cases have been described in monkeys, with convincing mineral studies. Notwithstanding so deep a background and so wide a scope it remained for Sir James Paget in 1877 to give clinical recognition to this disease, at first considered a rarity but with the development of diagnostic aids no longer so regarded.

*Incidence.* Schmorl, as a result of a series of post-mortem studies, quotes an incidence of 3 per cent in persons over 40 years, and at the Memorial Hospital, Coley states that they now routinely obtain skull plates on all patients over the age of 50 years seen in the Bone Tumor Clinic.

At the Henry Ford Hospital, from 1922 to 1937, in a total of 224,676 admissions, fifty-one cases were recognized, or one case of Paget's disease to every 4,500 admissions. Similar calculations from other clinics show an incidence of 1:3,000 to 1:16,000. In our own series only seventeen cases (33½ per cent) were recognized in the first half of the fifteen-year period and thirty-four cases (66½ per cent) in the remaining half. This is probably easily explained on the basis of rapid development of the x-ray as an aid in the diagnosis

of wholly unrelated conditions (Paget's disease being discovered only incidentally) as well as its more frequent employment in the differential diagnosis of bone diseases.

Kay, Simpson and Riddoch, in a series of ninety-six cases (sixty-two collected from the literature and thirty-four of their own), give 55 years as the average age of diagnosis with a range of 39 to 78 years. They show a sex distribution of fifty-nine males and thirty-seven females. Gutman and Kasabach, in an analysis of 116 cases, show an equal number of each sex with a general age range of 25 to 79 years. In the former group there were two siblings and in the latter series four cases reported a familial incidence (four members in one case). In our own group there were thirty-one males, with an average age when diagnosed of 57 years, and twenty females with an average age of 59.5 years, the total average age being 57.7 years. However, the age of onset is difficult to determine because of the mildness and indefiniteness of the early symptoms. (Table 1.) None of our cases

TABLE I  
DURATION OF SYMPTOMS (WHEN FIRST SEEN)

Duration	No. of Cases	Average Age
Less than 1 yr.....	7	60.7
1-5 yrs.....	13	60
6-10 yrs.....	10	58.7
11 yrs.....	5	57

gave a history of any other member of the family having the disease. Our age range was 40 to 77 years. Cases occurring as early as the second decade of life (12 to 16 years)

\* From the Henry Ford Hospital, Detroit.

have been reported, Paget himself reporting one as early as 28 years of age. These should probably be regarded critically as they may well represent osteitis fibrosa. That Paget's disease and osteitis fibrosa cystica may fortuitously occur together seems reasonable to suppose, and Aub has recently reported several such cases.

**Symptoms.** Pain seems to be the most distressing feature of the condition, confined usually to the lower extremities, back, and head, and it is usually the first symptom to appear. The pain in the long bones is constant in type and is often marked long before any clinical alteration can be detected. At first it may be due to periosteal stretching but later it is due to the new axes of strain and stress with the attendant ligamentous stretching incident to the bending. This is confirmed by the observation that the pain is much more prone to occur in the bones of the lower extremities than in those of the arms, the bending of course being more pronounced in the former. Back pain probably depends on the vertebral softening with compression (gravity) of the vertebral bodies, and on the postural deformity with the consequent stretching of the various groups of spinal ligaments. That it not infrequently leads to a different type of pain, namely that due to nerve irritation, is shown by the fact that in several of our cases there were periods of agonizing sciatica. One of our patients with spinal involvement had several attacks of herpes zoster. Arthritis is often a complicating factor. The headaches in patients with skull involvement are difficult to evaluate correctly due to the frequency of complicating hypertension and arteriosclerosis. Bending of the long bones is the result of softening, plus gravity and muscle pull. Other less common and for the most part self-explanatory signs and symptoms need not be commented upon and will merely be listed in the charts. (Table II.)

**Involvement.** The skull, spine, pelvis, femur and tibia are the bones most frequently involved, in the order named. In

the long bones the lesions generally first appear at the ends and later converge toward the midshaft. The periacetabular and sacroiliac regions appear to show the first signs of involvement in the pelvis. Apparently a slight predilection is shown by the disease for certain bones (i.e., ribs, scapulae, clavicles, etc.). This is

TABLE II

SIGNS AND SYMPTOMS (WHEN FIRST SEEN)

i. Skeletal:	
A. Long bones	
1. Deformity.....	20
2. Tenderness over or pain in.....	15
3. Increase in local heat.....	2
4. Overlying redness.....	1
5. Abnormal gait.....	4
B. Skull	
1. Deformity.....	7
2. Nerve deafness.....	5
Conduction deafness.....	1
3. Headaches.....	2
C. Miscellaneous	
1. Flaring of ribs and pelvis.....	2
2. Spinal deformity.....	6
3. Decrease in height or measurable bone shortening.....	8

also shown in groups of bones such as the vertebrae where the lumbosacral group predominates over the cervicodorsal. However, undue emphasis seems to have been placed on this, for when relative incidence is balanced by relative size of the bones this predilection becomes somewhat more apparent than real as an examination of most statistical tables, including our own, will show. (Table III.)

We are able to present an unusually high percentage of monostotic cases, twelve in all, or 24 per cent. The average age of this group was 57.7 years. Only three of these had symptoms dating as long as five years; four cases were admitted as fractures and five cases were asymptomatic, the diagnosis being based entirely on the roentgenologic picture. The tibia was involved in six cases, the skull in two, the humerus in two, the sacroiliac area in one, and the radius in one.

With regard to the roentgenologic appearance of the lesions little need be said. A heterogenous confluence of areas of osteoporosis and osteosclerosis with a predominance of the former in the earlier

and of the latter in the later stages, with a tendency toward overgrowth and thickening taking place as an integral part of the process, characterizes the x-ray picture.

The pathologic appearance of the lesions both grossly and microscopically is so well known as to need no elaboration.

TABLE III  
BONES INVOLVED

Bone	Totals	Author's Series	Packard, Steele and Kirkbude	Gutman et al.
Skull.....	154	23	49	82
Pelvis.....	136	25	21	90
Spine.....	137	24	31	82
Cervical } .....		{ 5	..	{ 5
Dorsal } .....		{ 9	..	{ 26
Lumbar } .....		{ 15	..	
Sacrum } .....		{ 13	..	{ 51
Femur.....	124	21	44	59
One } .....		{ 11	{ 4	
Both } .....		{ 10	{ 40	
Tibia.....	105	21	50	34
One } .....		{ 14	{ 3	
Both } .....		{ 7	{ 47	
Fibula.....	20	6	10	4
One } .....		{ 5		
Both } .....		{ 1		
Patella.....	13	4	8	1
One } .....		{ 2		
Both } .....		{ 2		
Humerus.....	68	10	21	37
One } .....		{ 6	{ 7	
Both } .....		{ 4	{ 14	
Scapula.....	27	3	6	18
Clavicles.....	45	0	31	15
Ulna.....	19	2	12	5
Radius.....	29	3	19	7
Hands.....	11	2	8	1
Ribs.....	29	5	16	8
Sternum.....	7	0	7	
Face.....	10	1	9	

**Biochemistry.** Decalcification, new osteoid tissue formation and inorganic salt deposition take place simultaneously in Paget's disease. The decalcification is more apt to predominate in the earlier and more active stages of the disease, the inorganic salt deposition in the later and less active stages. Hence it is inevitable that conflicting reports concerning calcium, phosphorus, magnesium, and sulfur balances should

have arisen (Locke, Hunter and DaCosta). The involved bones due to their large size show an increase in the total inorganic content, but the actual percentage inorganic content is less than normal.

Blood levels of calcium and phosphorus have quite generally been found to be within normal limits (Kay et al.; Gutman et al.). In our own series the blood calcium range was 9.0 to 10.6 mg. per cent, the blood phosphorus range was 1.72 to 4.54 mg. per cent with averages of 9.7 and 3.5 mg. per cent respectively. Any constant variations in the serum calcium depending on the stage of the disease (Belden and Bernheim) we were unable to observe.

The most recent additions to our knowledge of the biochemical changes taking place in Paget's disease have come from a study of phosphatase activity, begun by Kay in 1927. This substance, present in the plasma and enzymic in nature, possesses the property of hydrolyzing phosphoric esters such as glycerophosphate, hexosephosphate etc. The amount of this substance present is commonly expressed in Bodansky units, the normal value being 1 to 4 units.

The enzyme, insofar as has been determined, is a product of body cells in general but is present in the greatest concentration in the intestinal mucosa, kidney, and whole bone (Kay). In a few cases with a high plasma phosphatase concentration studied by Kay, the urinary concentration remained low. The excretion of this substance has been incompletely studied to date.

Bone lesions involving a fair portion of the skeleton are accompanied by a rise in the phosphatase content of the plasma. It has been found to be increased therefore in a number of conditions, including infantile and adolescent rickets (markedly increased) renal rickets, osteomalacia, osteogenesis imperfecta (normal or slightly increased), multiple myeloma (normal or slightly increased), osteogenic sarcoma, carcinoma with bone metastases, hyperparathyroidism and Paget's disease. Increased values have also been noted in diseases with

extensive liver damage. The highest values have been obtained however, in Paget's disease, they being higher than in osteitis fibrosa cystica for a comparable degree of bone involvement.

It is evident therefore that an increase in plasma phosphatase is the result rather than the cause of osteitis deformans, reflecting the cellular activity incident to osteogenesis. Consequently it is in itself of no value in differentiating Paget's disease from other conditions in which bone formation occurs. Coupled with roentgenographic evidence, however, it is a distinct aid in the diagnosis. In Paget's disease it may indicate the rate of development and is roughly proportional to the extent of involvement. Values as high as 120.6 units have been reported (Gutman) in patients with generalized bone involvement.

In our own group of cases phosphatase studies were carried out in sixteen cases

and averaged 12.74 units. (Table IV.) There were four monostotic cases in which the values ranged from 2.62 to 19.22 units with an average of 8.97 units. The case in which the value of 2.62 units was obtained three years later showed 5.49 units. The average of the polyostotic group was 13.9 units with a range of 5.83 to 30.15 units, somewhat low as compared with other series. Five of the sixteen cases were initially seen because of pathologic fractures. Contrary to what might be expected, it could not be stated that the phosphatase readings in these cases were any higher than in others showing a comparable degree of bone involvement. The small size of this group however precludes any dogmatism.

**Complications.** Many of these patients present coincident neuropsychiatric conditions and numerous degenerative eye changes have also been reported, but one would be going a bit far afield to attempt to place the blame for these on the disease under discussion. It is generally felt that these are due rather to coincident degenerative arterial changes. Knaggs, who has carefully studied the skull changes, states that the increase in the thickness of the skull takes place almost entirely outwards, and that the foramina are not seriously contracted, though the regularity of their margins (particularly the foramen magnum) may be impaired. Cranial nerve palsies can occur from compression, however. The commoner resulting conditions are optic atrophy and nerve deafness. The latter is the more frequent. Lindsay and Perlman, in a review of this subject, conclude that Paget's disease does not produce impairment in hearing except with extensive disease in the bones of the skull including the temporal bone, and that though it is capable of producing conduction deafness, that of the inner ear type is much more characteristic.

Fractures of the pathologic type occur in about 15 per cent of the cases. There were ten patients (20 per cent) presenting this complication in our series, one patient

TABLE IV  
PHOSPHATASE

Age	Duration of Symptoms (Years)	Extent of Involvement	Phosphatase
57	3.0*	+	7.48*
53	None*	+	19.22*
48	None*	+	8.98
42	6*	+	5.13*
61	None	+	2.62* (5-5-34) 5.49 (1-30-37)
51	1	++	8.21
57	1	++	7.35 (5-12-34) 4.06 (12-12-36)
52	None*	++	4.45 (12-2-35) 7.2 (2-9-37)
55	5	++	6.24 (10-9-36) 9.8 (1-25-37)
60	1	+++	8.64
72	7	++	11.9
63	5	+++	11.3
58	5	+++	20.4 (1-7-35) 14.3 (1-28-37)
51	None	++++	31.5 (8-14-35) 14.6 (11-26-35)
43	5*	+++	35.6 (3-28-34) 24.7 (12-17-34)
64	30	++++	35.05 (11-2-34) 20.8 (3-3-37)

\* Fracture.

having sustained two and another three separate fractures. It is common experience that with proper treatment these fractures heal well, with abundant callus formation and usually within normal time limits.

Calculi were found in four cases, two biliary and two urinary. Goldstein and Abeshouse, who have reported six cases of urinary calculi in Paget's disease, state that it is an infrequent complication. Aub states that the formation of urinary calculi in Paget's disease is less frequent than in osteitis fibrosa. Moehlig and Murphy in a recent publication report the high incidence of 15.6 per cent but in a series of only twenty-six cases.

Sarcomatous degeneration in bones involved in the osteitic process occurred in two cases. In the first case the tibia alone was involved and in the second, sarcoma appeared first in the femur and later in the radius. The incidence has been variously quoted at from 2 to 9.5 per cent (Speiser; Higbee and Ellis; Packard, Steele and Kirkbride; B. Coley and Sharpe). Codman states that 14 per cent of all Paget's disease patients succumb to osteogenic sarcoma. This association of the two conditions has not been found to occur under the age of 50 years. The average age of onset is 54 to 57 years, with males predominating. Our own two patients were 58 and 60 years of age respectively and both were females. Coley and Sharpe state that the Paget's is reported present one to twenty years before sarcoma develops. Due to the difficulty in rightly determining the onset of Paget's they felt that an interval of ten to fifteen years is more likely. The significance of this association is further emphasized by their statement that they know of no benign giant cell tumor or endothelial myeloma occurring in a bone that was the site of a preëxisting Paget's disease. In one of our cases there was a history of Paget's for only nine months and in the other for ten years. In seventy-one cases of osteogenic sarcoma over 50 years of age which Coley and Sharpe report (twenty of their own) there was an association with Paget's in 28 per cent. Kolodny found that 5 per cent

of all osseous sarcomas in the Bone Registry of the American College of Surgeons originated in bones involved in Paget's. In all cases of sarcoma of the skull there was preëxisting Paget's disease. Ochsner and Gage in thirty-one cases collected from the literature found more than one bone to be involved in eight cases (Coley and Sharpe in two cases).

The sarcoma is slightly different histologically from the usual uncomplicated osteogenic sarcoma in that it shows more giant cells and greater lymphocytic infiltration. The degree of malignancy is often greater also. Coley and Sharpe were unable to find any record of a patient surviving more than five years and Ochsner states that in all of the cases but one which he investigated death occurred within a few months. Our two cases lived only two and six months respectively from the time the diagnosis was made.

*Etiology.* Concerning the etiology of the disease little is known of a positive nature. That Paget himself considered it inflammatory in origin is indicated by the name, osteitis deformans, which he gave to it. Since then a heterogeneous group of factors among which are chronic absorption of intestinal toxins, lues, trauma, gout, rheumatism, malignant disease, trophic nervous disorders, heredity, and degenerative changes due to arteriosclerosis have been mentioned, all of which are probably incidental.

The disturbances in mineral balance accompanying Paget's disease, more particularly that of calcium, have been mentioned above. Whether they represent or are related to causes or to effects, however, can only be guessed at. The problem is not a simple one. The factors influencing calcium assimilation (Wagoner), the influence of magnesium intake (Kruse, Schmidt and McCollum), and vitamin D intake (Taylor and Weld; Watchorn; Pugsley and Anderson) not only on the calcium balance but also on the route of elimination deserve consideration.

The effect of the parathyroids on calcium metabolism is too well known to require

elaboration. Selye has been able to produce interesting bone changes in rats, characterized first by osteoporosis and later by osteosclerosis, by feeding large doses of parathormone. Bauer, Aub and Albright, as a result of their studies, suggest that hyperparathyroidism with its generalized stimulus for osteoclastic activity may enhance the localized unknown factor stimulating osteoclastic activity in Paget's disease. The interrelationship of calcium metabolism and thyroid function has also been established (Aub et al.; Hellwig; Klein; Pugsley and Anderson; Thompson; Hunter) and to complicate matters further the ability of thyroxin to sensitize the organism to parathormone might be mentioned (Stocker; Csépai and von Pellathy; Ask-Upmark). Moehlig, Murphy and Adler have attempted to correlate a high incidence of familial diabetes, familial tallness and obesity, and a high incidence of diabetic glucose tolerance curves with pituitary dysfunction.

However, in refutation it might be stated that patients with osteitis deformans generally exhibit normal appearing parathyroids; hyperthyroidism is an uncommon accompaniment of Paget's disease (Boothby and Sandiford; Wakely), amounting to only 6 per cent in this series; and Moehlig et al. were unable to produce any picture comparable to Paget's disease by the use of anterior pituitary extract in animals. In our own series only one case presented a family history of diabetes and although a family history of tallness and obesity was not regularly inquired into, these patients showed an average height and weight of 5 feet 6 inches and 152.4 pounds respectively for the males and 5 feet 1 inch and 145.5 pounds for the females, certainly not unusual.

**Treatment.** Treatment of a disorder as yet so little understood can be carried out with very little rationale and for the most part is merely symptomatic and palliative. Parathyroidectomy as well as the administration of parathormone have been tried with equally poor results. The administration of calcium, usually in combination

with vitamin D, in some form has been used with varying success, one of our own patients having followed such a regime for ten years with only indifferent results. X-ray often relieves the bone pain and proper orthopedic treatment during the stage of softening prevents much of the otherwise ensuing deformity.

Recently Gill and Stein have reported interesting results by using a diet low in calcium and phosphorus and high in magnesium, the magnesium being given in the form of magnesium carbonate. They measure the efficiency of the treatment by a lessening of the calcium and phosphorous retention, by a decrease of the plasma phosphatase, by a decrease in the density and diameter of the long bones, and by a subsidence of symptoms. They state that it seems likely that the magnesium exerts a favorable influence by increasing the solubility of calcium and phosphorus and because it acts as a vasodilator. However, they neglect to state which phases of the disease have been benefited by this treatment nor do they present any numerical report of the progress of the phosphatase readings.

Berman, postulating that the first stage of Paget's disease is due to a hyperfunctioning of the parathyroids in relation to a relative deficiency of the adrenal cortex, has tried administering extract of adrenal cortex. Over a period of six to twelve months he reports cessation of all symptoms with a recession of weakness and deformity. In twelve cases phosphatase determinations at monthly intervals showed a steady fall, usually to about one-fourth to one-seventh of the initial level (never became normal, however). We have not as yet attempted this method of treatment but feel that it does merit a trial.

#### SUMMARY

1. Fifty-one cases of Paget's disease are presented, representing an incidence of one in 4,500 admissions. The proportion of males and females was in the ratio of 3:2. The average age of onset was about 58 years with a range of 40 to 77 years.



2. Pain is usually the first symptom to appear, is usually the most distressing feature of the disease and is largely confined to the lower extremities and back.

3. The skull, spine, pelvis, femur and tibia are the bones most frequently involved and in the order named.

4. The x-ray picture presents a heterogeneous confluence of areas of osteoporosis and osteosclerosis with a predominance of the former in the earlier and of the latter in

10. The etiology remains obscure. There is little reason for implicating either the parathyroids, thyroid or pituitary.

11. The treatment is mainly symptomatic.

#### REFERENCES

1. ALBRIGHT, F., AUB, J. C., and BAUER, W. Hyperparathyroidism. *J. A. M. A.*, 102: 1276-1287 (April 21) 1934.
2. ASK-UPMARK, E. Thyrotoxicosis and tetany. *Endocrinology*, 16: 369-396 (July-August) 1932.
3. AUB, J. C., BAUER, W., HEATH, C., and ROPES, M. Studies of calcium and phosphorous metabolism; effects of the thyroid hormone and thyroid disease. *J. Clin. Investigation*, 7: 97-137 (April) 1929.
4. BAUER, W., AUB, J. C., and ALBRIGHT, F. Studies of calcium and phosphorous metabolism; study of bone trabeculae as readily available reserve supply of calcium. *J. Exper. Med.*, 49: 145-161 (Jan.) 1929.
5. BELDEN, W. W., and BERNHEIM, A. R. Clinical and therapeutic considerations of osteitis deformans. *Radiology*, 18: 324-348 (Feb.) 1932.
6. BERMAN, L. Endocrine treatment of Paget's disease. *Endocrinology*, 16: 109-119 (March-April) 1932.
7. BERMAN, L. Studies of Paget's disease; effect of adreno-cortical extract treatment upon the blood phosphatase in Paget's disease. *Endocrinology*, 20: 226-227 (March) 1936.
8. BODANSKY, A., and JAFFE, H. L. Phosphatase studies. III. *Arch. Int. Med.*, 54: 88-110 (July) 1934.
9. BOOTHBY, W. M., and SANDIFORD, I. Summary of basal metabolism data on 8,614 subjects with especial reference to the normal standards for the estimation of the basal metabolic rate. *J. Biol. Chem.*, 54: 783-803 (Dec.) 1922.
10. COLEY, B. L., and SHARPE, G. S. Paget's disease; a predisposing factor to osteogenic sarcoma. *Arch. Surg.*, 23: 918-936 (Dec.) 1931.
11. CSÉPAI, K., and VON PELLATHY, S. Ueber die parathormone-empfindlichkeit des menschlicher Körpers mit besonderer Riicksicht auf die Basedowsche Krankheit und die Hyperthyreosen. *Munchen. med. Wchnschr.*, 75: 813-814 (May 11) 1928.
12. DA COSTA, J. C., FUNK, E. H., et al. Study of the metabolism in osteitis deformans. *Proc. Path. Soc. Phila.*, 17: 29, 1915.
13. DA COSTA, J. C. Paget's disease of bones. *S. Clin. North America*, 1: 47 (Feb.) 1921.
14. DAVID, T. B., and COOKE, W. E. The supervision of osteogenic sarcoma in Paget's disease. *Brit. J. Surg.*, 25: 299-316 (Oct.) 1937.
15. DENNINGER, H. S. Paleopathological evidence of Paget's disease. *Ann. M. Hist.*, 5: 72-81 (Jan.) 1933.
16. ERDHEIM, J. Ueber die Genese der Paget's Knochenkrankung. *Beitr. z. path. Anat.*, 96: 1-60, 1935.
17. GILL, A. B., and STEIN, I. Bone metabolism; its principles and relations to orthopedic surgery. *J. Bone & Joint Surg.*, 18: 941-956 (Oct.) 1936.

TABLE V  
INCIDENTAL LABORATORY DATA

Chemistry	No. of Cases	High	Low	Average
N.P.N	21	41 6	12 6	32 5
Sugar	22	105	65	74
Uric acid	5	3 77	2 82	3 17
Urea	4	16 4	10 7	13 7
P.S.P	11	68	28	57
Calcium	20	10 6	9 0	9.7
Phosphorus	29	4 52	1 72	3 5
Glucose tolerance	7			
Increased	1			
Decreased	5			
Normal	1			
B.M.R	14			
Minus 10-15	1			
Plus-minus 10	8			
Plus 10-15	2			
Plus 30-40	3			

the later stages with a tendency toward bone overgrowth and thickening.

5. A negative calcium and phosphorus balance is generally present in the earlier and more active stages of the disease and a positive calcium balance in the later and less active phases, but the blood calcium and phosphorus levels are normal throughout.

6. The plasma phosphatase is usually increased in Paget's disease. It may indicate the rate of development and is roughly proportional to the extent of involvement.

7. Fractures occur in about 15 per cent of cases, but tend to heal well and within normal time limits.

8. Calculi are not common, occurring in four of the present series.

9. Sarcomatous degeneration is not uncommon, may occur in multiple foci and is generally rapidly fatal.

18. GILLIAN, G. J. Osteitis deformans. *Canad. M. A. J.*, 17: 60-63 (Jan.) 1927.
19. GOLDSTEIN, A. E., and ABESHOUSE, B. S. Urinary calculi in Paget's disease. *Am. J. Surg.*, 30: 359-368 (Nov.) 1935.
20. GRATZ, C. M. Pathological fractures. *S. Clin. North America*, 10: 565-576 (June) 1930.
21. GUTMAN, A. B., and GUTMAN, E. B. Paget's disease: relative constancy of serum phosphatase levels over periods up to 2 years. *Proc. Soc. Exper. Biol. & Med.*, 33: 150-153 (Oct.) 1935.
22. GUTMAN, A. B., and KASABACH, H. Paget's disease. *Am. J. M. Sc.*, 191: 361-380 (March) 1936.
23. GUTMAN, A. B., TYSON, T. L., and GUTMAN, E. B. Serum calcium, inorganic phosphorus and phosphatase activity in hyperparathyroidism, Paget's disease of bone. *Arch. Int. Med.*, 57: 379-413 (Feb.) 1936.
24. HELLWIG, C. A. Iodine deficiency and goiter. *Arch. Path.*, 11: 709-722, 1931.
25. HUNTER, P. Studies in calcium and phosphorus metabolism in generalized diseases of bones. *Proc. Roy. Soc. Med.*, 28 (11): 1619-1638 (Oct.) 1935.
26. KAY, H. P. Phosphatases of mammalian tissues. *Biochem. J.*, 22: 855-866, 1928.
27. KAY, H. P. Plasma phosphatase in osteitis deformans and in other diseases of bones. *Brit. J. Exper. Path.*, 10: 253-256 (Aug.) 1929.
28. KAY, H. P., SIMPSON, S. T., and RIDDOCH, G. Osteitis deformans. *Arch. Int. Med.*, 53: 208-248 (Feb.) 1934.
29. KLEIN, J. E. Effect of calcium on storage of colloid in thyroid gland. *Ann. Int. Med.*, 7: 1080-1083 (March) 1934.
30. KLEIN, J. E. New concepts in etiology and treatment of thyroid disease. *Arch. Pediat.*, 53: 233-242 (April) 1936.
31. KNAGGS, R. T. On osteitis deformans and its relation to osteitis fibrosa and osteomalacia. *Brit. J. Surg.*, 13: 206-237 (Oct.) 1925.
32. KOLODNY, A. Bone Sarcoma. Chicago, 1927. Surgical Publishing Co. (quoted by Ochsner).
33. KRUSE, H. P., SCHMIDT, M. M., and MCCOLLUM, E. V. Studies on magnesium deficiency. *V. J. Biol. Chem.*, 106: 553-572 (Sept.) 1934.
34. LINDSAY, J. R., and PERLMAN, H. B. Paget's disease and deafness. *Arch. Otolaryng.*, 23: 280-287 (May) 1937.
35. LOCKE, E. A. Osteitis deformans (Paget's disease). In *Oxford Medicine*, 4: 408. New York, 1921. Oxford University Press.
36. LOW, M. B., WILSON, R. O., and AUB, J. A. Phosphatase activity of the bones and kidneys in thyrotoxicosis. *Proc. Soc. Exper. Biol. & Med.*, 31: 447-450 (Jan.) 1934.
37. MOEHLIG, R. C., and ADLER, S. Carbohydrate metabolism disturbance in osteoporosis and Paget's disease. *Surg., Gynec. & Obst.*, 64: 747 (April) 1937.
38. MOEHLIG, R. C., and MURPHY, J. M. Attempt to produce Paget's disease by the use of anterior pituitary extract and parathyroid extract. *Am. J. Roentgenol.*, 34: 465-474 (Oct.) 1935.
39. MOEHLIG, R. C., and MURPHY, J. M. Paget's disease. *Endocrinology*, 19: 515-522 (Sept.-Oct.) 1935.
40. MOORE, S. Observations on osteitis deformans. *Am. J. Roentgenol.*, 10: 507-518 (July) 1923.
41. OCHSNER, A., and GAGE, I. M. Osteogenic sarcoma developing on osteitis deformans. *S. Clin. North America*, 10: 851-868 (Aug.) 1930.
42. PACKARD, F. A., STEELE, I. P., and KIRKBRIDE, T. S. Osteitis deformans. *Am. J. M. Sc.*, 122: 552-569 (Nov.) 1901.
43. PAGET, J. Additional cases of osteitis deformans. *Proc. Roy. Med. & Chir.*, 9: 147, 1882.
44. PHILIPS, H. B. Paget's disease. *J. Bone & Joint Surg.*, 8: 643-650 (July) 1926.
45. PUGSLEY, T. I. Effect of parathyroid hormone and irradiated ergosterol on calcium and phosphorus metabolism in rat. *J. Physiol.*, 75: 315-328 (Nov. 5) 1932.
46. PUGSLEY, T. I., and ANDERSON, E. M. Effect of desiccated thyroid, irradiated ergosterol and ammonium chloride on the excretion of calcium in rats. *Biochem. J.*, 28: 754-758, 1934.
47. PUGSLEY, T. I., and ANDERSON, E. M. The effect of administration of calciferol on increased calcium excretion induced by thyroxine. *Biochem. J.*, 28: 1313-1315, 1934.
48. RABINOWITCH, I. M. Metabolic studies in a case of osteitis deformans. *J. Nutrition*, 5: 325-346 (July) 1932.
49. ROBERTS, R. E., and COHEN, M. J. Osteitis deformans (Sect. electro therapeutics) *Proc. Roy. Soc. Med.*, 19: 13-40 (March) 1926.
50. SELYE, H. On stimulation of new bone formation with parathyroid extract and irradiated ergosterol. *Endocrinology*, 16: 547-558 (Sept.-Oct.) 1932.
51. SCHMORL, G. Über Osteitis deformans Paget. *Virchows Arch. f. Path. Anat.*, 283: 694-751, 1932.
52. SPEISER, F. Sarkomatöse Entastung bei Osteitis deformans. *Arch. f. klin. Chir.*, 149: 274-295, 1928.
53. STOCKER, H. Thyroxin and Parathormone bei postoperativer Tetanie. *Deutsche Ztschr. f. Chir.*, 222: 357-373, 1930.
54. TAYLOR, N. B., and WELD, C. B. Mobilization and excretion of calcium following overdosage with irradiated ergosterol. *Brit. J. Exper. Path.*, 13: 109-127 (April) 1932.
55. THOMPSON, J. Influence of calcium on thyroid gland of albino rat. *Arch. Path.*, 16: 211-225 (Aug.) 1933.
56. WAGONER, G. Present views of calcium-phosphorus metabolism. *Am. J. M. Sc.*, 191: 511-515 (April) 1936.
57. WAKELEY, C. P. G. Paget's disease of the humerus and clavicle, associated with Graves' disease. *Proc. Roy. Soc. Med.*, 26: 47-48 (Nov.) 1932.
58. WATCHORN, E. Irradiated ergosterol and phosphorus metabolism. *Biochem. J.*, 24: 1560-1563, 1930.
59. WHITE, E. P. G. Osteitis deformans in monkeys. *Arch. Int. Med.*, 30: 790-796 (Dec.) 1922.
60. WOODARD, H. Q., and HIGINBOTHAM, N. L. The correlation between serum phosphatase and roentgenographic type in bone disease. *Am. J. Cancer*, 31: 221-237 (Oct.) 1937.

# A SIMPLIFIED METHOD FOR PRODUCING A WINDOW CAST

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**M**AKING a window in a plaster cast has always been a time consuming procedure, and frequently, the

can be rounded or moulded and, since a smooth edge will not absorb as rapidly as a rough cut edge, it will remain clean longer.

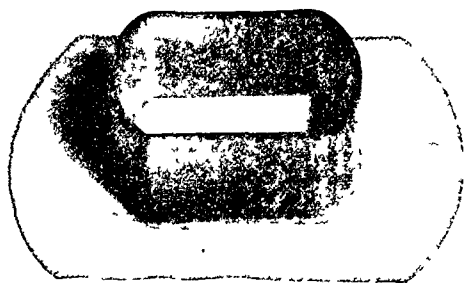


FIG. 1. The rubber collar is extremely heavy, but pliable. The flange is very thin and easily moulded to the part.

effort to protect the wound permitted an area of enlarged cast to allow an undue amount of edema. If padding had to be used, that which remained after the window was constructed quickly soiled, and thus an early change of cast was necessary. If the window was large, extra thickness of plaster was necessary to reinforce the remaining part, thus producing a heavy unwieldy cast.

In an effort to simplify this procedure, we present a rubber collar with a thin flange which fits directly over the wound and allows the wet plaster to be applied around the collar, thus constructing a window at the time of the application. The rubber will not adhere to the plaster, and by forcefully removing the collar with an upward pull before the plaster is completely set, there is produced a slight elevation around the edges of the window which permits the dressing gauze to be placed within the cast. This manipulation does not loosen the cast in its full diameter. After the collar has been withdrawn the edges



FIG. 2. A moulded window demonstrating the smooth edges.

Should it be desired, the rubber flanges can be made adherent to the skin with colodion, so that the rubber collar can be left intact after application thus permitting the use of wet dressings. Window casts made with this collar are applied directly to the skin.

The application is simple where a small window is necessary, but with the larger collars the plaster bandage is applied by carrying it back and forth, from lateral edge to lateral edge. When the proper thickness has been acquired a few longitudinal strips are laid down. On the removal of the collar the up-turned edges are folded outward and smoothed.

The upright edges of the collar are sufficiently strong to allow manipulation without folding, while the flanges are thin enough to permit conformation to the part. The whole collar is made of live rubber. Plaster does not stick to this material. After use the collar can be cleansed with water and kept as any other rubber equipment.

We are indebted to the American Anode Company for constructing the experi-

mental collars. They can be obtained in any length or width. For the average wound a 2 inch width gives ample working space. Due to the raised area immediately surrounding the window the space need not be excessively large as in the case of the cut window or where a box top is used.

The advantages of the rubber collar are:

1. Ease of application.

2. Ability to apply a form fitting cast without padding.

3. The application of a light weight window cast without weakened areas.

4. Early moulding of the edges of the window, thus assisting in keeping the cast clean longer.

5. Walling off of the wound by leaving the collar intact permitting freedom of treatment.



THE victim of a spinal injury complicated by paraplegia must never be lifted by the shoulders and hips in such a way that the spine sags between the points of support. . . . The face down position is relatively safe, for the spine is then hyperextended, and in most spinal fractures hyperextension reduces the displacement and relieves cord compression.

From—"Fractures and Other Bone and Joint Injuries" by R. Watson-Jones (Williams and Wilkins).

# BLADDER DISTURBANCES IN DISEASES OF THE SIGMOID\*

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**O**BSERVATIONS at the Carney Hospital during the past several years have emphasized the importance of urinary tract manifestations in diseases of the sigmoid. These observations prompted the writers to review the cases of diverticulitis and malignant disease of the sigmoid admitted to the hospital between January 1, 1928 and January 1, 1938.

Bladder disturbances in these disease entities are logical to expect, in view of the anatomic proximity of the two organs. Vesical involvement may be the result of direct extension and actual invasion or may be due to external pressure on the bladder by the pathologic process. A factor of significance is the relative fixity of the bladder which makes it an accessible locus for the spread of disease from the relatively mobile sigmoid. This likewise explains in great measure the infrequency of large bowel invasion by primary malignant disease of the bladder even though actual peritoneal extension is frequently observed.

Manifestations of urinary tract involvement in sigmoid disease show a preponderance in the male. The protective influence of the uterus, which rests between the bowel and the bladder in the female, functions as an impenetrable barrier so that pathologic communication between the two organs becomes anatomically quite difficult. Another factor is that diverticulitis and malignant disease of the sigmoid, the most common offending diseases, occur more frequently in the male.

A review of the literature reveals that the first reference to the subject appeared in 1843 when Barbier de Mille discussed the operative intervention of vesico-intestinal fistula. Isolated reports appeared at variable intervals thereafter until 1909 when Parham and Hume reviewed the literature

and presented an excellent treatise on the subject. Chute, Cunningham, Keefe and Hinman have contributed to the literature since that time. In 1935, Colby reported definite adhesions to the bladder in 13 per cent of a series of seventy-seven cases of malignant disease of the sigmoid. In 1936, Higgins reviewed 328 cases of vesico-intestinal fistula from the literature and added thirty-five cases from the Cleveland Clinic. He found that ninety-six cases were secondary to diverticulitis of the sigmoid and thirty the result of sigmoid malignancy.

Our study disclosed that sixty-six patients with diverticulitis of the sigmoid were admitted to the Carney Hospital over a period of ten years, thirty-two of whom were males and thirty-four females. The youngest was 31 years of age and the oldest 85. Thirty-six patients, or 55 per cent, had definite urinary complaints; eighteen associated their symptoms with those referable to the large bowel. The chief complaint was in twelve instances consistent with pathology in the urinary tract. Pain simulating left ureteral colic was encountered in two patients, probably the result of impingement of the left ureter by an inflamed diverticulum or abscess. Urinary frequency, hematuria, terminal dysuria, urgency and gas and feces in the urine were other complaints. Localized scrotal pain was the only symptom in two instances. Definite vesico-intestinal fistulae were encountered in three patients. Bladder inspection was made in seven individuals.

It is worthy of note that two of our medical colleagues are subject to intermittent attacks of diverticulitis. They have experienced definite vesical disturbances consisting of urgency, frequency and severe urethral pain at the end of urination,

\* From the Urological and Surgical Services, Carney Hospital, Boston. Read at the Diamond Jubilee Celebration of the Carney Hospital on May 17, 1938.

probably the result of the contiguity of an inflamed diverticulum.

In our series there were thirty-seven cases of malignant disease of the sigmoid, ranging in age from 24 to 76 years. There were sixteen males and twenty-one females. Subjective urinary complaints were present in eight instances. The presenting complaint was referred to the urinary tract in one instance. There were two vesicointestinal fistulae. A comparison of these findings reveals that diverticulitis played a greater rôle in the development of urinary symptoms than carcinoma.

The intimate relationship between the field of the urologist and the problems of the gastroenterologist and abdominal surgeon are here illustrated. Chute has written that "long-continued, left-sided abdominal pain or discomfort, followed by bladder irritation as the diverticulum becomes attached to that organ, and finally the occurrence of the opening of the diverticulum into the bladder with apparent anuria and followed by the presence of gas and feces in the bladder at times, is the classical picture of diverticulitis with vesico-intestinal fistula."

Recognition of diverticulitis in the early stages is quite difficult as in most instances, it is insidious, obscure, and practically symptomless. There may be some constipation or lower left abdominal discomfort to which the patient may attach no real significance. As the disease progresses, especially during an acute exacerbation, pain may become more marked and a complaint of tenderness on pressure may be present. Objective findings of muscular spasm and the palpable evidence of a mass may make the diagnosis less difficult. The clinical features may be so distinctly urologic that the victim may first consult a urologist because of symptoms of vesical irritation. The consultant may find that the symptoms are out of proportion to the findings or the study of the urinary tract may be absolutely negative. In this group, the fact that an early extra-urinary lesion may reflect itself in the urinary tract must be kept in mind. Disease in the sigmoid

must not be overlooked. A careful history of bowel habit must be obtained and special diagnostic procedures carried out to exclude pathology in the sigmoid as the chief factor in the patient's complaints.

The severity of the urinary tract manifestations depends upon the type of pathology present. In diverticulitis, as the inflammatory process develops and the sac becomes distended by acute inflammation, a peridiverticulitis develops. If it rests in proximity to the bladder, disturbances of urination may result. If the mass subsides spontaneously, as it does in many instances, the clinical signs and symptoms may regress or disappear. In the chronic recurrent type, the vesical disturbances may recur. If the process progresses to definite suppuration, the development of a fistula between the two organs is imminent. Attention may not be directed to the presence of a fistula until long after the communication has been established, as the opening may be so minute as to preclude the possibility of fecal and gaseous passage into the bladder cavity. In most individuals, however, an acute inflammatory reaction is set up in the bladder and the patient presents the symptoms of an acute cystitis and in some instances the clinical picture of pyelonephritis with chills, fever, and toxemia. With the appearance of a definite open channel or tract, gas and fecal material are passed through the urethra or the patient may develop a pseudo-anuria with the passage of urine per rectum. The fistulous tract may be a direct communication or a long tortuous sinus. The latter is observed more frequently in the inflammatory type while the direct communication is more characteristic of the malignant group.

Secondary vesical involvement by malignant disease of the sigmoid may result from direct invasion of the bladder by the cancerous process and ultimate fistula formation or be due to the development of an inflammatory process around the tumor which becomes adherent to the bladder, as in diverticulitis, and finally may form a fistula.

The clinical recognition of this group depends on the proper evaluation of the signs and symptoms plus the physical findings correlated with special diagnostic measures including cystoscopy, proctoscopy and x-ray studies. The cystoscopic picture varies with the extent of the disease, the presence or absence of fistula and the sex of the subject.

Distortion of the left lateral wall of the bladder due to extravesical pressure is the earliest manifestation of urinary tract disturbances. This finding must be evaluated with care, particularly in the female as other causes must be excluded. A pelvic examination must be made to exclude pathology in the female genital system. As the process advances toward the bladder and becomes adherent to it, the bladder picture is altered. Localized areas of increased vascularity with submucosal hemorrhage followed later by edema are noted. In the presence of tumor the reaction in the bladder is more localized and as further invasion takes place a definite tumor may be seen projecting into the bladder. There may or may not be ulceration.

The end stage of this whole process as far as the bladder is concerned is the development of a fistula. In the earliest stage it may be so minute that its cystoscopic recognition is not only difficult but in many cases impossible.

Primary malignancy of the bladder must be excluded in this group of cases and in some instances biopsy may be necessary. The differential diagnosis between diverticulitis and malignant disease is often extremely difficult. It is our impression that the vesical reaction in the former is more fulminating than that due from extension of cancer. Barium enema is the important diagnostic procedure. In a definite percentage of cases preoperative diagnosis may be impossible and surgical exploration alone may solve the problem. Delineation of the fistulous tract may be obtained in some instances by left lateral cystogram or by barium enema, and its presence actually confirmed by finding dye, such as methylene blue, in the rectum or stool following

its injection into the bladder, or the presence of barium in the bladder following a barium enema.

The treatment of the urinary tract complications in diseases of the sigmoid should be directed to the eradication of the primary disease. The type of therapy medical or surgical, is dependent upon the pathology present and the stage in which it is encountered. General measures should be instituted to combat urosepsis and maintain renal values. If a fistula is present, the fecal stream should be diverted by colostomy to protect the upper urinary tract from further infection. Following this procedure, the inflammatory process (if present) may subside and the spontaneous closure of the fistula may occur. Later plastic procedures, however, often are necessary. Excision of the primary disease should never be carried out during the acute stage.

#### SUMMARY

Cases of diverticulitis and malignant disease of the sigmoid admitted to the Carney Hospital over a ten-year period are reviewed. The high incidence of vesical disturbances is emphasized. The frequency of such disturbances is shown to be greater in diverticulitis than in malignant disease. The clinical manifestations may be distinctly urologic in this group. The close coöperation among the urologist, the abdominal surgeon and the gastroenterologist in the management of disease of the sigmoid is essential.

#### REFERENCES

1. BARBIER DE MILLE. Cited by Parham and Hume.<sup>2</sup>
2. PARHAM, F. W., and HUME, J. Vesico-intestinal fistulae. *Ann. Surg.*, 50: 251, 1909.
3. CHUTE, A. L. Diverticulitis of the sigmoid as a source of bladder irritation. *J. Urol.*, 21: 13, 1929.
4. CUNNINGHAM, J. H. Rectovesical and enterovesical fistulae. *Surg., Gynec. & Obst.*, 21: 510, 1915.
5. KEEFE, J. W. Diverticulitis of the sigmoid or pelvic colon with sigmoidovesical fistula. *Boston M. & S. J.*, 194: 569, 1926.
6. COLBY, F. H. Cancer of the colon involving the bladder. *Tr. Am. Soc. Genitourinary Surg.*, 28: 199, 1935.
7. HIGGINS, C. C. Vesico-intestinal fistula. *J. Urol.*, 36: 694, 1936.

# TREATMENT OF GRANULOMATOUS PROCTITIS OF LYMPHOPATHIA VENEREUM

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**B**ENIGN stricture of the rectum associated with lymphogranuloma inguinale has been investigated and established in etiology, pathogenesis, and diagnosis. Therapeusis, while on a non-specific basis, has been favorably reported in the literature. All measures instituted, are individualized. Direct methods are effected towards alleviation of symptoms and prevention of complications.

Benign stricture is relatively common. All the therapeutic measures attack the pathologic entity of the chronic ulcerating stenosing proctitis, (stricture) and periproctitis in the terminal stages of the lymphogranuloma inguinale, but there remains the granulomatous proctitis, the treatment of which is inadequately discussed in the cases reported. This granulomatous proctitis persists after the procedures employed to rectify the benign stricture.

Several of the methods popularly utilized consist of either enlargement of the lumen of the stricture by plastic operations or dilatation. Temporary colostomy, a radical type of treatment, is still in use by some.

Granulomatous proctitis is usually found above and below the stricture. It may extend as far down as the linea dentata. To the palpating finger, the mucosa is thickened like a band, or indurated and corrugated. There is a marked delineation between the involved and the non-involved lumen. On proctoscopic examination the membrane is edematous and covered with whitish viscid purulent or sanguinopurulent secretions. When these are wiped away, the mucosa is pale and granular, with a tendency to bleed. The glands and the interglandular connective tissue are thickened. Ulcerated lesions are localized in area, but may show a marked depth in penetration.

The presence of proctitis is almost constantly associated with a seropurulent or mucopurulent discharge from the rectum.

Before discussing the treatment of granulomatous proctitis, it should be reiterated that the benign inflammatory stenosis, annular or tubular, should be attacked by the local methods mentioned previously. The decision obviously will rest on the surgical judgment of the physician and the extent of the pathology. Where surgical treatment is decided on, incisions which are carried to the verge are conducive to better drainage and aid in accelerating a good end result in the subsequent treatment of the granulomatous proctitis. For those cases which require dilatation, it may be well to remember that the proper sized proctoscope is an invaluable dilator, as the field is envisioned before the insertion of the obturator of the instrument. Irrespective of the method of attack, general anesthesia is contraindicated.

Immediately after the stenosis has been relaxed, incised or excised, the following formula is applied topically to the granulomatous proctitis, above and below:

Tincture iodine.....	30 c.c.
Menthol.....	0.65 Gm.
Tincture benzoin comp.....	50 c.c.
Glycerine.....	20 c.c.

These applications are made daily until the third day when deep heat is introduced in conjunction with them, and continued for ten days. Then the deep heat is continued alone, but the interval is lengthened to three times weekly for two weeks, and twice a week for one month.

Diathermy was found to be the only satisfactory method for producing deep heat. Picard<sup>1</sup> explains that diathermy,



because it generates sufficient heat, causes a revitalization of granulomatous tissue. The active electrode is a Hegar bougie just sufficient to pass the site of the treated stricture without pain. The method is simple and safe if the amperage is not excessive. Excessive amperage may provoke some hemorrhage early in the treatment of the congested membrane, but this is easily controlled. A current of one ampere for an exposure of ten to fifteen minutes will suffice to keep the intensity of heat in the granulomatous area averaging 40°C. grade. Length of individual treatments can

be varied according to the severity of the condition.

The functional results and the local response were satisfactory. Treatment does not interfere with the adjuvant procedures of daily irrigations of medicated or non-medicated solutions to be used by the patient to keep the bowels clean. The technique is presented in the hope that more extensive trials will be made and its value determined.

#### REFERENCE

1. PICARD, HUGO. Diathermiebehandlung der Strictures Recti. *Zentralbl. f. Chir.*, 52: 1709 (Aug.) 1925.



EXPERIENCE . . . has shown that the best results are obtained if blood is withdrawn, stored and distributed from special centres equipped for the purpose. It is easier to ensure adequate sterility of apparatus and methods of collection when trained personnel work in suitably equipped institutes.

From—"War Wounds and Air Raid Casualties" (Lewis).

# SURGICAL MANAGEMENT OF DUODENAL ULCER<sup>+</sup>

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IN considering the surgical treatment of duodenal ulcer, it is first necessary to determine the indications for operation since the ulcer of itself is not necessarily a surgical condition. Medical treatment alone may suffice to control it.

The chief indication for the surgical treatment of duodenal ulcer is perforation; the second, obstruction. Substitution of surgery for medical treatment may also be indicated for certain complications, chief of which is hemorrhage, especially when recurring under good medical management; persistence of the symptoms and failure of the ulcer to heal, as demonstrated roentgenologically after medical treatment; or roentgenologic evidence of marked induration of the ulcer (such ulcers rarely heal even with the best medical management). Blahd<sup>1</sup> has found that if an ulcer shows a crater formation, and a small amount of barium is retained in the depths of the crater, it is intractable to medical treatment and operation should be performed.

When surgical treatment is clearly indicated, the question arises as to the type of operation which is most appropriate and expedient. While in continental Europe subtotal gastrectomy has been the operation of choice for many years, in England and America most surgeons employ gastroenterostomy in the majority of cases.

In 1935, Fogelson<sup>2</sup> presented a review of the literature (covering the year 1933) on surgical treatment of gastroduodenal ulcerative disease, and called attention to the excellent results obtained with gastrectomy by European surgeons, especially Finsterer and von Haberer, but he did not mention any American surgeon as an advocate of this operation. In 1934,

however, Richter<sup>3</sup> found "a widening circle of accepted indications for gastric resection of peptic ulcer" in American literature. In 1937, when Fogelson<sup>4</sup> again reviewed the literature (for 1934 and 1936), he found a growing sentiment in favor of gastrectomy in England and America. He mentioned Ogilvie in England, Graham in Canada and Hinton and Lahey in the United States as advocating gastric resection in most cases of gastric and duodenal ulcers. In the last two years, reports by American surgeons on the favorable results of gastrectomy in peptic ulcer have become more frequent.<sup>5-9</sup> Cutler and Zollinger<sup>10</sup> are also now of the opinion that subtotal gastrectomy is the optimum procedure in many cases of peptic ulcer.

The employment of partial gastrectomy has been based largely upon personal observations of unfavorable sequelae resulting from gastroenterostomy. Gastric resection so frequently gives permanent relief that it is here advocated as the operation of choice. Where the condition of the patient is such as to preclude his withstanding a lengthy and highly technical operative procedure, gastroenterostomy is resorted to as an emergency measure.

Gastroenterostomy may be indicated in certain specific instances, such as cases with relatively low gastric acidity and with marked stenosis of the pylorus, especially when due to scar tissue and adhesions. Such findings are more often observed in elderly patients. Here gastroenterostomy is preferable to subtotal gastrectomy because it entails less risk and is a less radical procedure.

Where the ulcer is on the anterior wall of the duodenum, the ulcer-bearing area

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is resected and a subtotal gastrectomy performed. If the ulcer is on the posterior wall of the duodenum, the ulcer-bearing

repeated small blood transfusions where there is anemia.

Spinal, local, block, and splanchnic anes-

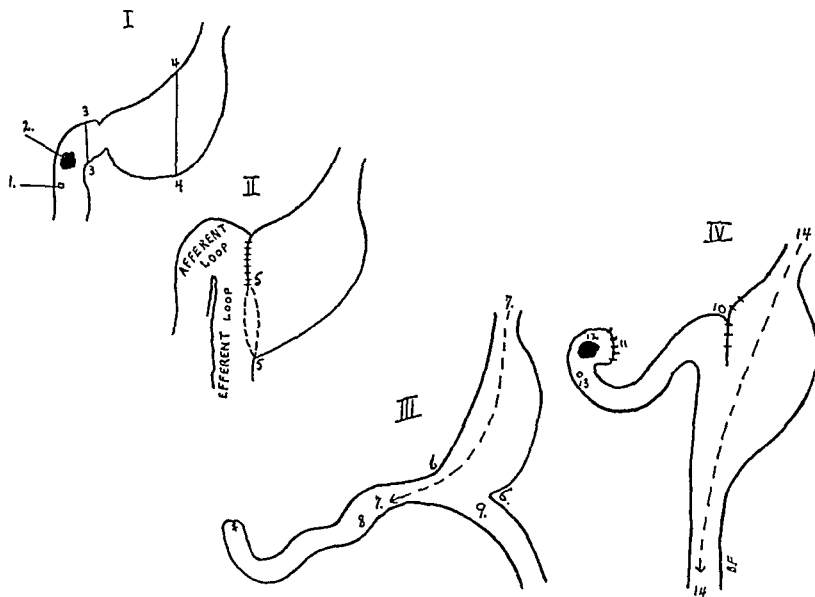


FIG. 1. 1, papilla. 2, ulcer. 3, line of resection at pylorus. 4, line of resection of stomach. 5, 5, anastomosis—partial breadth of stomach; upper portion closed and attached to jejunum. 11, patient with Polya-Reichel resection, in upright posture. 6, anastomosis of entire breadth of stomach without angle sutures. 7, direction of food current. 8, afferent loop of jejunum (giving rise to retrograde filling) lower than efferent loop, 9. iv, patient with Finsterer resection, in upright posture. 10, obliteration of three angled corner, fixing afferent loop of jejunum at higher level than efferent, preventing retrograde filling. 11, pylorus closed with Lembert sutures. 12, ulcer. 13, papilla. 14, direction of food current into proper efferent channels.

area is similarly resected, if possible, and a subtotal gastrectomy performed. Should the ulcer be bound down and adherent to the underlying pancreas, careful dissection of the ulcer from the pancreas, close to the duodenal wall, is carried out, the rent closed, subtotal gastrectomy performed and drainage instituted. If the penetrating ulcer extends outward toward the papilla or if the callus infiltration of the ulcer is so extensive that the common bile duct cannot be isolated, the Finsterer resection operation for exclusion<sup>11</sup> is resorted to. If the first part of the duodenum is free, the pylorus is removed to insure adequate and safe closure of the duodenum.

Since operation for duodenal ulcer is not an emergency procedure except in perforation, the patient can be prepared by rest, administration of fluids, gastric lavage (if there is food retention) and

thetia has been used, but inhalation anesthesia of nitrous oxide, oxygen and ether has been found preferable and satisfactory in this series.

#### TECHNIQUE

A midline incision is made, long enough to give sufficient exposure for the entire operative field. The stomach and duodenum are examined to determine the exact location of the ulcer. If necessary, the exact localization of an ulcer of the posterior wall can be determined by a small gastrotomy opening in the antrum into which the palpating finger is inserted and through which the duodenal wall is explored. The Cameron light may facilitate visualization of a duodenal ulcer where palpation may fail to locate it.

By slightly elevating the liver the gastro-hepatic omentum is made taut. Through a

rent in the avascular area of the latter, the middle finger and forefinger of the left hand are inserted, exploring the entire area

angles to the body axis of the stomach itself. A Payr clamp is applied parallel to and about two fingerbreadths distal to the

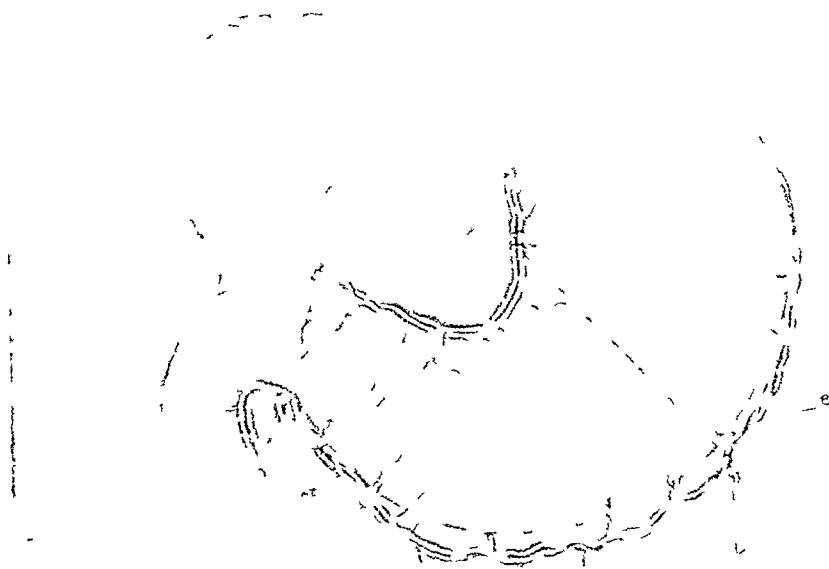


FIG. 2. Blood supply of stomach. *a*, gastric artery. *b*, pyloric artery. *c*, right gastroepiploic artery. *d*, left gastroepiploic artery. *e*, dotted line shows area of gastric resection. Points of ligation marked on vessels

behind the stomach down to the greater curvature. The right and left gastroepiploic arteries are ligated close to the stomach. Mass ligation is to be avoided in order to protect the blood supply of the omentum. The gastrocolic ligament is detached from the stomach, on the right as far as the duodenum, on the left about a handbreadth beyond the middle of the greater curvature. The blood vessels of the lesser curvature are ligated and two silk ligatures are applied to the blood vessels at the re-entrant angle. The lesser omentum, including the hepatoduodenal ligament, is divided.

A slit is made in the transverse mesocolon close to the left of the middle colic artery. The edges of the slit are secured by means of two guide sutures. About 10 cm. distal from the ligament of Treitz the proximal end of the jejunum is marked by a silk suture. A von Haberer stomach clamp is applied to the stomach at the point where resection is desired and at right

stomach clamp. A moist pad is placed behind that area of the stomach which is to be resected and the stomach cut across close to the Payr clamp. This may be accomplished by the knife or cautery. The distal portion of the resected stomach is covered with a moist pad and reflected for the time being away from the operative field.

The left flap of the split transverse mesocolon is sutured to the posterior wall of the stomach in the operative field. The marked end of the jejunum is now brought through the split in the transverse mesocolon and two traction sutures are applied on the jejunum including the stomach at points directly opposite the remains of the lesser and greater curvatures. The first suture opposite the lesser curvature is inserted at the marked end of the jejunum by means of a fine silk serosal suture. The entire posterior wall of the stoma is attached in this fashion to the longitudinal axis of the jejunum between the traction

sutures. Where the stoma of the stomach is larger than desired a through-and-through suture of o chromic catgut is carried from

prevention of retrograde filling. This could not occur by the method presented.

In cases where the stomach is contracted,



FIG. 3. A, von Haberer stomach clamp applied to stomach. Traction sutures applied on jejunum including stomach at points directly opposite remains of lesser and greater curvatures. Through-and-through chromic catgut No. o suture in stomach from lesser towards greater curvature, closed; stomach now no greater than four fingerbreadths. Opening of jejunum directly opposite and same length as stoma of stomach. B, duodenum closed by two Connell inversion sutures. Lesser omentum and capsule of pancreas sutured over the line of closure on duodenum.

the lesser toward the greater curvature until the stoma is no greater than four fingerbreadths. This is reinforced by a Lembert suture of linen or silk. An opening in the jejunum is made directly opposite and the same length as the stoma of the stomach. A through-and-through lock chromic catgut o suture is used in closing the anastomosis of the jejunum to the stomach. This is reinforced by the original serosal suture of silk or linen. The line of anastomosis is now covered by the right split half of the transverse mesocolon by interrupted sutures.

The procedure just described precludes the necessity of inserting the safety sutures of Finsterer at the lesser curvature for the

partial closure is at times inadvisable. In such instances the opening in the jejunum is made to equal the length of the opening in the stomach. In this case two or three angle sutures of fine silk or linen are inserted at the lesser curvature of the stomach to attach the jejunum to the stomach in such manner as to prevent angulation of the jejunum with ensuing closure of the anastomosis or retrograde filling.

The postoperative occurrence of retrograde filling merits serious attention in the consideration of the operative procedure to be followed. In the event that retrograde filling does occur as the result of food traversing the afferent loop instead of the

effluent loop of the anastomosis, the backward pressure in the resected stump may eventually give way, with an ensuing

anastomosis, left to the last, has been done in haste. When resection is left to the last, and the condition of the patient precludes

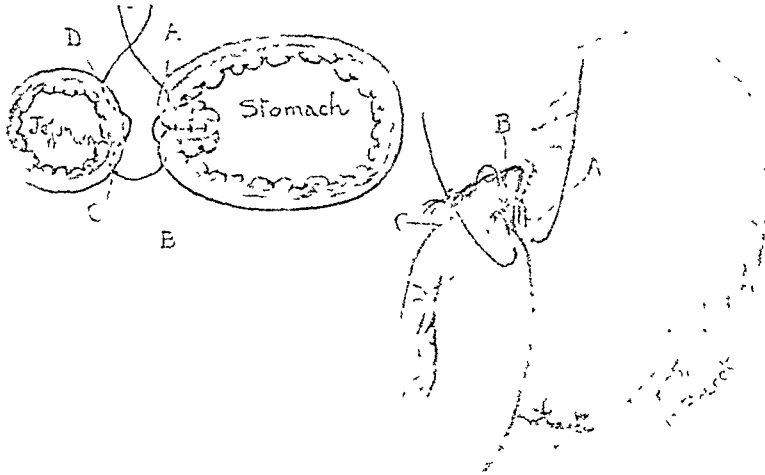


FIG. 4. Polya-Reichel resection. Entire breadth of stomach opening anastomosed to jejunum. A, B, C, D, angle suture of Finsterer for the prevention of retrograde filling. (Anterior wall of stomach, posterior wall of stomach, posterior wall of jejunum, anterior wall of jejunum. Three such sutures inserted.)

fatality. In nonresectable ulcers the misdirected chyme, constantly bathing the ulcerated area, prevents its ultimate healing and causes persistence of the original symptoms. The remaining right leaf of the split transverse mesocolon is sutured by means of interrupted linen or silk sutures, covering the line of anastomosis.

Frequently a Levine tube is utilized in the course of this operation. The tube is inserted a day or two before the operation for repeated lavage. When the stomach is resected the tube is pulled up a few inches from the operative field; after the anastomosis is completed the tube is pushed down into the jejunum for 6 inches and left in situ for about four days. This facilitates the administration of fluids, if necessary, and withdrawal of excessive secretions should they be present.

Instead of resecting the distal portion of the stomach first and then completing the anastomosis as the final stage in the operation, the procedure is reversed. In the method above described one is immediately able to visualize the pancreas and the structures behind the stomach. At times the condition of the patient is such that the

proper termination of the operation, the distal end can be rapidly closed. Resection and removal of this end of the stomach may be completed at some other time when the patient's condition allows.

The reflected end of the distal portion of the stomach and ulcer-bearing area permits the proper visualization and palpation of the pathologic tissues. If it is decided that the duodenal ulcer can be removed, the duodenal ligaments are separated for about 2 cm. beyond the ulcer-bearing area and all bleeding points ligated, with care not to injure the bile ducts. At this point the duodenum must be separated from its underlying attachment to the pancreas. The gastroduodenal artery, if encountered, must be ligated. The pancreas is dissected away from the duodenum to the point of the ulcerated area. Two traction sutures are applied to the upper and lower borders of the duodenum beyond the ulcerated area and a clamp is applied distal to the ulcer. A small opening is made beyond that into the anterior duodenal wall, through which suction is used for the removal of duodenal contents. This opening is then enlarged and the duodenum is cut across,

freeing it from the ulcer-bearing area. The severed duodenum is closed by inverting it with two rows of fine silk suture, using the Connell stitch. A third row is used to bring the lesser omentum and capsule of the pancreas over the anterior portion of the duodenum.

Where the ulcer on the posterior wall of the duodenum is bound and adherent to the underlying pancreas, dissection is carried out as close to the duodenal wall as possible in order to avoid injuring the pancreatic ducts. The ulcer-bearing area is thus left behind, attached to the pancreas, and is cleansed with alcohol. The rent in the duodenal wall is closed and a soft rubber dam drain is inserted over the ulcerated area left behind. The operative procedure is carried out as described above. The duodenal stump is buried as interrupted sutures of fine silk or linen are taken into the edges of both hepatoduodenal and hepatocolic ligaments.

On the other hand, when the ulcer is so situated that it cannot be resected, either because of its location, its extensiveness or its adherence to the important underlying structures—pancreas, liver and gall-bladder—the resection operation by exclusion must then be utilized. The gastroduodenal ligament is detached about two fingerbreadths proximal to the pylorus, and the same is done with the lesser omentum. Between two clamps the antrum is severed from the pylorus, unless the ulcer is located in the descending portion of the duodenum near the papilla. In this instance the pylorus is removed in addition to the antrum, the duodenum being severed close to the pylorus. The distal portion is closed with a through-and-through suture reinforced by a Lembert of silk or linen. The stump is then covered with gastroduodenal ligament and a portion of the lesser omentum. Gastrojejunostomy is completed according to the method previously described, closing the abdomen with drainage. In the resection operation “by exclusion” the gastrojejunostomy may be left to the last because no time and effort are lost in

the separation of the ulcerated, bound down and adherent duodenum to the underlying structures. There is no necessity for haste and for reversing the process, as described above in the operation of subtotal gastrectomy above.

#### COMMENT

It is at once apparent that the point of contention is the relative desirability of gastroenterostomy or subtotal gastrectomy. Many surgeons consider the latter procedure too radical for a condition that may be alleviated by simple gastroenterostomy. However, experience has shown that in capable hands subtotal gastrectomy need present a mortality no higher than gastroenterostomy. Ogilvie<sup>12</sup> states that a patient with a gastroenterostomy may be happy, but he is never safe. Ulceration at or near the stoma follows in at least 20 per cent of the cases. Such a complication may require one of the most difficult technical operations in the realm of surgery, and is attended by a mortality as high as 19 per cent. Ogilvie assumes that 5 per cent is a fair average for gastroenterostomy mortality. However, if 18 per cent of the survivors develop marginal ulceration and ensuing operative procedures result in a mortality of 22 per cent, the total death rate following gastroenterostomy will eventually be not 5 per cent, but 9 per cent. Therefore, subtotal gastrectomy in the hands of a skilled surgeon would eventually reduce the mortality by 4 per cent.

Ginzburg and Mage,<sup>13</sup> in a review of eighty-six cases of failures following gastroenterostomy, stated that though an efficient stoma in the gastroenterostomy tends to bring about the healing of an active duodenal ulcer, it also seems to favor the development of a marginal ulcer. They observed that the changes produced in an active duodenal ulcer by gastroenterostomy produced not a cure, but rather a remission of signs and symptoms.

In favor of subtotal gastrectomy it may be said that a patient is better off with a part of the stomach functioning normally than

with the whole stomach functioning abnormally. Furthermore, the removal of that portion of the stomach which bears the greater percentage of acid-bearing glands eliminates to a decided extent one of the main provocative factors of ulcer formation. While anastomotic ulceration may also take place in subtotal gastrectomy, experience has shown that when this occurs it is usually due to the fact that not enough of the acid-bearing area has been removed.

Lahey<sup>14</sup> has written: "In my mind jejunal ulcer is too frequent, too difficult and too dangerous a postoperative sequela for gastroenterostomy to be employed as a routine method of treating duodenal ulcer." Walters,<sup>15</sup> however, favors the more conservative method of gastroenterostomy, claiming that results are equally good.

Fogelson,<sup>4</sup> in his extensive review of the literature of gastroduodenal ulcerative disease for the years 1934-1936 draws the conclusion that the surgeon himself should select that type of surgical intervention which in the light of his own previous experience has been most satisfactory to him.

Eggers<sup>16</sup> seems to be averse to subtotal resection in duodenal ulcer. He advocates resection when repeated, especially massive hemorrhages, have not been controlled or after failure of conservative operations or for intractable pain, and possibly for gastrojejunal or jejunal ulcer.

It may also be possible that many more cases of jejunal ulcer may follow a gastroenterostomy than is reported from the larger clinics. It is often difficult to make comparisons. Statistics from the various clinics are equally confusing. One must not lose sight of the fact that death rates often considered as the result of operation are not directly caused by such operations. These may merely be contributing factors, for the functional unity of heart, lungs, kidneys and other vital organs is not the same in all patients subjected to gastroenterostomy or subtotal gastrectomy. The age, occupation,

physical habitus, preoperative preparations, postoperative care and innumerable extraneous factors play an important rôle in the morbidity and mortality rate in gastric surgery.

It is for these reasons that a vital factor in the determination for the type of operation desired is not only the recognized indication for surgery but also the previous experience of such surgery in the hands of the operator.

I am indebted to Drs. John J. McGrath and Robert E. Brennan, Professors of Surgery, New York Polyclinic Medical School and Hospital, for their helpful suggestions.

#### REFERENCES

1. BLAHD, M. E. Surgical indications for peptic ulcer and its surgical management. *Surg., Gynec. & Obst.*, 62: 203, 1936.
2. FOGELSON, S. J. Gastroduodenal ulcerative disease. *Surg., Gynec. & Obst.*, 60: 1, 1935.
3. RICHTER, H. M. Gastric resection for peptic ulcer. *Surg., Gynec. & Obst.*, 59: 337, 1934.
4. FOGELSON, S. J. Gastroduodenal ulcerative disease. *Surg., Gynec. & Obst.*, 65: 1, 1937.
5. GRAHAM, R. R. Technical surgical procedures for gastric and duodenal ulcer. *Surg., Gynec. & Obst.*, 66: 269, 1938.
6. MILLER, G. Subtotal gastric resection for peptic ulcer. *Surg., Gynec. & Obst.*, 65: 489, 1937.
7. LAHEY, F. H., and MARSHALL, S. R. The surgical treatment of peptic ulcer. *New England J. Med.*, 217: 933, 1937.
8. MARSHALL, S. F., and KIEFER, E. D. Partial gastrectomy for gastric or duodenal ulcer. *J. A. M. A.*, 109: 1341, 1937.
9. WALTERS, W. Should gastric resection be done for duodenal ulcer? *Surgery*, 2: 759, 1937.
10. CUTLER, E. C., and ZOLLINGER, R. Surgery of the stomach and duodenum; procedures for peptic ulcer and gastric ulcer. *Surg., Gynec. & Obst.*, 67: 318, 1938.
11. FINSTERER, H. The surgical treatment of duodenal ulcer. *Surg., Gynec. & Obst.*, 52: 1099, 1931.
12. OGILVIE, H. W. The place of surgery in the treatment of peptic ulcer. *Lancet*, 228: 419, 1935.
13. GINZBURG, L., and MAGE, S. Failures following gastroenterostomy for gastroduodenal ulcer. *Surg., Gynec. & Obst.*, 67: 6, 1938.
14. LAHEY, F. H. Peptic ulcer-gastric, duodenal and jejunal. *S. Clin. North America*, 15: 1401, 1935.
15. WALTERS, W. Operative treatment of gastric and duodenal ulcers: physiological and pathological principles influencing the type of procedure. *J. Michigan State M. Soc.*, 35: 491, 1936.
16. EGERS, C. Gastro-enterostomy. *Ann. Surg.*, 108: 84, 1938.
17. LEVIN, A. L. *J. A. M. A.*, 76: 1007, 1921.



# A NEW PHYSICAL SIGN USEFUL IN THE EARLY DIAGNOSIS OF PERFORATED DUODENAL ULCER

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**D**IMINISHED liver dullness occurs in a great majority of patients suffering with acute perforation of the duodenum as an important early sign. This diminution may begin a few minutes after perforation, the usual time for a complete obliteration varying from one to three or four hours. I have observed cases in which the decreasing area of liver dullness was graphically portrayed by horizontal lines drawn to contact the retracting edge every thirty minutes. Associated with this there is usually demonstrable free fluid in the peritoneal cavity.

The average time between onset of symptoms and admission to the hospital in cases of perforated duodenal ulcer is over twelve hours. In the majority of cases, therefore, liver dullness has been obliterated before hospitalization. The demonstration of this sign depends upon the interchange of position between the air and the free fluid in the peritoneal cavity.

*Method of Examination for Sign.* The patient is placed in the supine position and the liver area percussed. If only partially obliterated, the exact area of liver dullness is outlined with ink, but in the majority of cases, obliteration will be complete. The patient is then requested to turn on his abdomen. He may object because of the exaggeration of the intense pain by any attempt to change position, in which case he should be helped over and asked to remain so for two or three minutes.

He should then be placed on his back; the area of liver dullness can then be definitely outlined. If this area is repeatedly percussed at short intervals, dullness will be gradually replaced by tympany. It usually takes from one to three minutes for air to replace the fluid which suggilates to the dependent part of the peritoneal cavity.

While the diagnosis of acute perforation of the duodenum can usually be made from the history, and the board-like rigidity that accompanies it, it is very difficult at times to differentiate it from acute pancreatitis and high intestinal obstruction. Likewise, when a duodenal perforation is subacute, it is difficult to differentiate it from early fulminating appendiceal perforation.

In both acute pancreatitis and high intestinal obstruction, free fluid may be demonstrated, but of course, air will be absent from the peritoneal cavity. In subacute perforation of the duodenum and in the fulminating appendiceal perforation, gas is usually not present in sufficient quantity to be of definite importance.

Aside from its diagnostic significance, the demonstration of this sign will lessen the financial burden to the hospital, as well as to the patient. The customary flat x-ray plates made of the abdomen to demonstrate the presence of air beneath the diaphragm in cases of questionable diagnosis will not be necessary.



# APPENDICITIS INDUCED BY TRAUMA

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OVER the last decade, discussions of appendicitis induced by trauma have been appearing in the surgical journals with more frequency. Nearly each discussion has spoken with the increasing weight of authority of the preceding articles cited. An editorial in the *Journal of the American Medical Association* concludes, "The pertinent question is not whether trauma can originate an initial attack of appendicitis, or whether its effect is that of lighting up dormant pathologic conditions. It is, rather, whether or not trauma can precipitate a clinical attack of acute appendicitis. The consensus is not only that it can, but that the resulting attack is likely to be one of a grave, destructive type, with a clear clinical picture. Usually, after a blow on the abdomen, a kick, a fall, or a sudden muscular strain, severe abdominal pain occurs followed by vomiting. The initial pain and vomiting are characteristic and are presumably due to intraperitoneal shock. Then, in most cases, as pointed out by Behan, both symptoms cease and return later, as the result of the progression of inflammatory changes within the abdomen."

After having read the five references appended to this editorial as well as many other references beginning with Kelly's exhaustive monograph published in 1905, this writer believes it would be well to pause and reconsider the cases which have been reported in the literature before endorsing the view taken in this editorial.

Boyd, in discussing the etiology of appendicitis, brings out well known facts which most of the articles ignore: "It is a curious fact that although appendicitis is such a very common disease the etiological factors still remain vague and indefinite. The frequency of the disease is only of recent date. Appendicitis was present but was relatively rare, in highly civilized

communities until the end of the nineteenth century. Since that time it has become very common in these countries. The rise began in England about 1895, and was pronounced between 1895 and 1905; since then it has been fairly stationary. It was in the cities and amongst the better off classes that the rise was most marked; inmates of institutions on a plain diet are relatively immune.

"The national distribution of the disease is very interesting. It is common in the highly civilized countries such as Great Britain, the United States, France and Germany. In Denmark and Sweden it is lower. In Spain, Greece, Italy, and the rural parts of Roumania it is very low. Lucas-Championnière found one case of appendicitis in 22,000 patients among Roumanian peasants, whilst in the cities of Roumania he found one case in every 22 patients. McCarrison states that during the nine years that he practiced among the hill tribes of Northwest India he never saw a case of appendicitis. In Asiatics, Africans, and Polynesians it is very rare, unless they take to European food; then it becomes common. In wild animals it is rare or unknown. In animals in captivity it is common, especially among the apes in zoological gardens.

"Rendle Short points out that the link connecting these various facts may be found in the absence of cellulose and fiber from modern civilized food. It was between 1890 and 1905 that the chief change occurred, owing partly to the greater importation of food stuffs."

The exciting cause is equally elusive. Indeed, although foreign bodies such as oxyuris or concretions are occasionally found, and adhesions and kinks may obstruct the appendix, in the majority of

cases it is impossible to say what has precipitated the attack.

The editorial previously mentioned concluded that the trauma might be direct, such as a blow to the abdomen, a kick or a fall on the abdomen, or the pinioning of the abdomen against a fixed object, or indirect resulting from prolonged muscular strain or untoward or unusual sudden muscular action. Overdistention of the organ by the influx of cecal contents as the result of trauma was regarded as the most plausible cause of traumatic appendicitis. However, in the light of what we know about the etiology of appendicitis, the theory is not very plausible. In many of the cases the patients were financially interested in establishing trauma as the cause of their disease. This makes it improbable that a true history of the development of the illness was given.

Among the inciting traumatic causes given in the literature most of the activities which make up our daily lives have been named: walking, dancing, running, stooping, lifting, falling. When we consider that the hill tribes of northern India stoop, run, ride beasts of burden, fall, fight, and probably even dance their own steps, without developing appendicitis, it seems improbable that these activities, which for many people make up existence itself, could be the cause of acute appendicitis as we know it, i.e., (1) acute catarrhal appendicitis where the infection commences at the mucosal lining and probably invades the walls to a variable extent, and where resolution may be complete, or where some residual scarring may be left; (2) acute diffuse appendicitis where the infection commences at the bottom of one of the crypts, and may extend throughout the organ and may result in acute gangrenous appendicitis.

In acute appendicular obstruction we have some slight pathologic evidence to support the case of trauma as a contributing cause. Wilkie has emphasized the importance of distinguishing between two varieties of acute appendicular disease,

namely, acute appendicitis and acute appendicular obstruction. The end result may be the same, but the method of production, the mode of onset, and the early clinical symptoms are different. In primary acute inflammation the pathologic process commences essentially as an inflammation of the wall of appendix. In primary acute obstruction, on the other hand, the essential lesion is the obstruction; the inflammation follows as a secondary consequence.

The peculiarity about the onset in acute appendicular obstruction is that at first the symptoms are purely local, and it is not until later that the general signs of inflammation manifest themselves. The important features distinguishing primary obstruction from primary inflammation are: (1) the great severity of the pain; (2) the suddenness of its onset; and (3) the absence of disturbance of the pulse and temperature during the early stages of the illness. This absence of what are regarded as important indications of appendicular disease may be very misleading, but it must be realized that if acute inflammation of the appendix is a serious condition, acute obstruction is even more so and calls for equally immediate operation.

The predisposing causes of acute obstruction are: (1) fibrous stenosis of the appendix; and (2) acute kinking of the appendix by a band or a fold. Fibrous stenosis is due to some previous attack of inflammation, which often passes quite unrecognized; the narrowing of the lumen at the proximal end may be so extreme that only a pinhole is left. A band or a fold which causes fixation of the appendix at some point is a common cause of obstruction. Such a band may be an old inflammatory adhesion but even more frequently it is a congenital fold which ties the middle of the appendix down toward the pelvis.

The exciting cause is a sudden access of fecal material to the partially obstructed appendix. This sudden access may be theoretically the result of straining or of some form of trauma, the latter being a

not infrequent precursor of an attack of acute appendicular obstruction. We may theorize that a slight reaction occurs in the distal part of the appendix, and the associated swelling rapidly intensifies the obstruction or accentuates the kink. In some cases a concretion is found beyond the obstruction, and the irregular peristalsis of the appendix may drive it into the narrowed part, thus rendering the obstruction complete.

Wilkie has shown in a very interesting way the effect of varying conditions on an isolated loop of ileum, the ends of which were closed. (1) When the loop was empty, it became distended with mucus until a mucocoele developed. (2) When the loop was moderately full of fecal material, the animal having been fed on a carbohydrate diet, an empyema of the loop gradually developed. (3) When the loop was full but the animal had been fed on a rich protein diet, the changes were much more acute, and the animal was dead within twenty-four hours.

The analogy to the conditions found in the human appendix is obvious. When the empty appendix becomes completely obstructed the result is a hydroperitonitis or mucocoele of the appendix. When the obstructed appendix contains some fecal material, probably not rich in protein, an empyema of the appendix gradually develops. Those common cases where distention and gangrene come on with startling rapidity correspond to the condition in the artificial appendix filled with feces after protein feeding.

Reference has already been made to the prevalence of acute appendicitis in civilized communities and in cities as compared with uncivilized communities and rural districts. Speaking generally it may be said that in the former proteins are consumed, in the latter carbohydrates. Post-mortem statistics suggest that fibrosis and scarring due to mild attacks of inflammation are common in all nations, but the urgent gangrenous type is confined to the meat-eating peoples. Acute appendicular disease is more than twice as common in the male as the female. This may, within the limits of possibility, be due to the fact that the young adult male is more subject to strain and trauma, and that his diet is usually richer in protein than that of the female. Finally, the acute form is rare in the first years of life and in old age. In the former obstruction cannot readily occur, whilst in the latter the lumen is often obliterated by fibrotic changes.

#### CONCLUSIONS

While it seems theoretically possible that trauma may occasionally be a factor in acute appendicular obstruction, it is probable that it is very infrequently so, because it is rare among these people living under the peasant conditions of Europe and the tribal conditions of India who eat meat plus an unrefined diet, and who are subject to trauma in all its forms.

I acknowledge indebtedness to Boyd's "Surgical Pathology" for much of the above material.



# APPENDICEAL OXYURIASIS\*

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APPENDICEAL oxyuriasis is a disease found the world over, although its frequency varies considerably in different parts of the globe. In France, Brumpt<sup>1</sup> studied 800 cases and found the oxyuris in 3.4 to 5 per cent. Ralliet<sup>2</sup> found the worm in 1.4 per cent of thirty-three organs removed, and a second time, in fifty-eight of 119 appendices examined. From Germany, Suzuki<sup>3</sup> in 500 autopsies and 103 surgically removed specimens found thirty-eight cases in the first group and sixteen in the second series. Fisher<sup>4</sup> reported forty-six instances in a series of 110 surgically removed specimens, and in 105 post-mortem cases found the oxyuris in thirty-nine. Castellani<sup>5</sup> quotes Garrison's figures at 8 per cent for the Philippines; Dobson's<sup>6</sup> at 15.37 per cent for India. Wood<sup>7</sup> reports from Australia seven cases in fifty-seven extirpated organs. Gordon<sup>8,9</sup> in this country, in 26,051 specimens from the University of Michigan, found 311 cases. In England, Still<sup>10</sup> found the worm in thirty-eight of 200 consecutive autopsies on children under 12 years of age. A second report by this author presented thirty-two additional cases in 100 necropsies on children between 2 and 12 years. Eastwood<sup>11</sup> found twenty-eight instances in a series of 123, seventy-three of which were operative organs and fifty post-mortem specimens. On the other hand, Crile<sup>12</sup> failed to record a single instance in 1,000 surgically removed appendices. Deaver<sup>13</sup> found the worm once in 500 operated organs.

The disease was first mentioned by Still in 1899. Since then there has been considerable controversy as to whether the worm is the causative factor in the production of acute appendicitis. The opinion has been

sharply divided into three schools: those who believe that there is a definite relationship between the worm and inflammation of the organ (Metchnikoff,<sup>14</sup> Rheindorf,<sup>15,16,17</sup> Cecil and Buckley,<sup>18</sup> Riff,<sup>19</sup> Harris and Brown,<sup>20</sup> Innes and Campbell,<sup>21</sup> Suzuki<sup>3</sup>); those who doubt the ability of the worm to produce an inflammatory reaction (Aschoff,<sup>22,23,24</sup> Hueck,<sup>25</sup> Brauch,<sup>26</sup> Fisher,<sup>4</sup> Drigalski and Koch,<sup>27</sup> Eastwood,<sup>11</sup> Steichele,<sup>28</sup> Wood<sup>7</sup>); a third group is of the opinion that the parasite is capable of producing minute lesions in the mucosa of the appendix, thereby permitting fecal matter to enter, resulting in inflammation (Jaroschka,<sup>29</sup> Ssolowjew<sup>30</sup>).

Of late, however, the opinion among most pathologists is that the worm is not the causative factor in the production of an acute inflammation. In Gordon's series, the largest on record, not a single case was found in which the oxyuris could be said to play a rôle. In this series, Gordon studied eight acute appendices, four acute purulent and two acute gangrenous organs. The worms were present, but never was there any evidence of involvement of the mucosa. At no time did he find a more severe or advanced degree of inflammation at the level containing the oxyuris than occurred in areas free of the worm.

It has been a common experience to find, in the amputated appendix harboring the worm, that the parasite has penetrated the wall. There is much to prove that the act of penetration took place after the organ had been removed, for there is no evidence of tissue reaction surrounding the worm. Many of these appendices showed hyperplasia of the lymphoid tissue, fecal concretions, dilatation of the lumen, atrophy and

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chronic catarrh of the mucosa, or combinations of these changes. According to Warthin,<sup>31</sup> such findings are classified as "no active process."

The disease occurs most commonly in children between 2 and 16. A case in a 69 year old male is found in Gordon's report. Female children are the victims three times more often than males.

The eight cases we are reporting offer a good cross section of the literature on oxyuris appendicitis. In this group there were six females and two males. The oldest was 17, the youngest 6.

*Duration of Symptoms.* Six were sick twenty-four hours before entering the hospital. One was ill for two and one-half days before surgery was instituted. The eighth child was operated upon after an illness of three days.

*Previous Attacks.* One-half of this series gave a history of previous attacks of abdominal pain. Two complained of repeated attacks for two years; two had had attacks for over a year, whereas the fifth offered a question as to previous manifestations.

*Temperature.* All the patients entered the hospital with some rise in temperature. The highest was 102 degrees, the lowest 99.8 degrees. On admission five of the children had a temperature of 100 degrees. One entered with a reading of 105, but a concomitant chest condition accounted for the acute rise.

*Nausea and Vomiting.* Seven complained of nausea. Vomiting from one to three times occurred in six patients.

*Abdominal Pain.* All complained of some type of abdominal pain. Six stated that the onset was with diffuse or periumbilical pain, later localizing to the right lower quadrant. In two the onset was with pain in the right lower quadrant.

All complained of tenderness in the right lower quadrant.

*Rigidity.* This phenomenon presented itself in 50 per cent of the cases, being especially found over McBurney's area. One child showed doubtful spasm, whereas

in two others no mention is made of the finding.

Rebound tenderness was present in only one instance.

Distention was noted once.

*White Blood Count and Differential.* The highest count was 13,900, the lowest 5,800. One child was admitted with a 31,200 count, but a complicating pneumonia was the responsible factor. Six had a marked increase in polymorphonuclear leucocytes, the highest being 86 per cent. It is interesting to note that in the only instance in which the pathologist made a diagnosis of acute ulcerative appendicitis, the white count was 8,800, with 49 per cent polymorphonuclear leucocytes.

*Bowels.* Diarrhea was a symptom in one case. One was constipated, whereas the others gave no story of change in bowel habits.

*Preoperative Diagnosis.* A preoperative diagnosis of acute appendicitis was made seven times. In the eighth case there was a history of repeated attacks of acute abdominal pain for two years. On several occasions a diagnosis of acute appendicitis had been made. Operation was advised because of these recurrent attacks.

*Operative Findings.* Free fluid in the abdominal cavity was found five times. Two appendices had bulbous tips. Two contained fecoliths. An edematous organ was reported twice.

Three organs were diagnosed as acute appendicitis by the operating surgeon. One was called an obstructive appendicitis, another, a chronic interval appendix; the others were considered as subacute specimens.

*Pathologic Report.* Only one of the cases was reported as having any evidence of acute inflammation. All others were reported as containing the oxyuris.

*Stool Examination.* After the worms were discovered, the stools of four patients were examined. The worm was isolated once; eggs were found in one instance, whereas in the other two the stools were negative.

There was one death in this series. The patient was a 6 year old male who entered the hospital after a three day illness. On admission his temperature was 105 degrees, the white count was 31,200, of which 88 per cent were polymorphonuclear leucocytes. Peri-umbilical pain at the onset was followed shortly by a chill. At the hospital the child was extremely toxic, very dyspneic, coughed considerably and had a marked expiratory grunt. Examination of the chest showed evidence of a bilateral pneumonia. The entire abdomen was markedly rigid, with exquisite pain and tenderness in the right lower quadrant. The pediatrician felt that in addition to the pneumonia the child had an acute appendicitis, and urged removal of the appendix. This was done under local anesthesia, and a slightly injected appendix was removed. Subsequently the boy developed an empyema, with blood cultures positive for type 4 pneumococcus. Death occurred on the seventh postoperative day. Autopsy showed a pneumothorax and collapse atelectasis of the left lung; empyema and post-pneumonic atelectasis of the right lobe; bronchopneumonia; oxyuris in the appendix. No active process was demonstrated in the amputated organ.

In reviewing the literature as well as from these cases, one is impressed with the fact that almost invariably the preoperative diagnosis is acute appendicitis. The abdominal pain, the frequency of nausea and vomiting, the slightly elevated temperature, the tenderness and frequent rigidity in the right lower quadrant, the increased white cell count, the increase in the polymorphonuclear leucocytes, all make for this diagnosis. Many of the symptoms and findings are most difficult to explain. Aschoff believed that the activity of the worm, acting as a foreign body might cause painful contractions of the muscular wall and produce pain. Can this explain the rigidity? If, as believed by many pathologists, the worm cannot produce an active inflammation, how then can we explain the rise in temperature, the

increase in white count, the polymorphonuclear leucocyte increase? Some investigators have expressed the thought that the oxyuris produces a toxin. This may, perhaps, explain some of the symptoms. It is obvious, nevertheless, that no symptom or absence of symptoms of appendiceal oxyuriasis can distinguish the disease from a true appendicitis.

#### SUMMARY

1. Eight cases of appendiceal oxyuriasis are presented.
2. Seven were diagnosed as acute appendicitis.
3. No symptom or lack of symptoms will differentiate the disease from a true acute appendicitis.
5. Removal of the appendix cures the patient.

#### REFERENCES

1. BRUMPT, E. Précis de parasitologie. Paris, 1913. Masson.
2. RALLIET, G. Sur les parasites de l'appendice malade. *Comp. rend. Soc. de biol.*, 70: 310, 1911.
3. SUZUKI, K. The rôle of oxyuris vermicularis in the etiology of appendicitis and allied conditions. *Surg., Gynec., & Obst.*, 21: 702-721, 1915.
4. FISHER, W. Oxyuten und appendicitis. *Deutsche Ztschr. f. Chir.*, 183: 222-245, 1925.
5. CASTELLANI, A., and CHAMBERS, A. J. Manual of Tropical Hygiene. New York, 1919. Wm. Wood.
6. DOBSON, A. Cited by Castellani.<sup>5</sup>
7. WOOD, W. A. Appendicopathia oxyurica. *M. J. Australia*, 1: 234-235, 1918.
8. GORDON, H. Appendiceal oxyuriasis and appendicitis. *Arch. Path.*, 16: 177-194, 1933.
9. GORDON, H. Appendiceal oxyuriasis. *Ann. Int. Med.*, 4: 1521-1534, 1931.
10. STILL, G. F. Observations on oxyuris vermicularis in children. *Brit. M. J.*, 1: 898-900, 1899.
11. EASTWOOD, E. H. The relation between appendicitis, oxyuris vermicularis and local eosinophilia in the appendix wall. *J. Path. & Bact.*, 26: 69-81, 1923.
12. CRILE, G. W. A summary of 1000 cases of appendicitis with observations on the etiology. *Ohio State M. J.*, 2: 615-617, 1906-1907.
13. DEEVER, H. C. Appendicitis in childhood, with a report of 500 cases. *J. A. M. A.*, 55: 2198-2205, 1910.
14. METCHNIKOFF, L. Rôle des helminthes dans l'appendicite. *Jour. d. Praticiens*, Paris, 15: 185, 187, 1901.
15. RHEINDORF, A. Ueber die durch die Oxyuris Vermicularis hervorgerufenen pathologisch-anatomischen Veränderungen in der Wand des

- Wurmfortsatzes nebst Betrachtungen ueber die Genese und das Vorkommen der Appendicitis. *Frankfurt. Ztschr. f. Path.*, 14: 212-266, 1913.
16. RHEINDORF, A. Hysteroneurasthenie oder chronische Appendicitis? Zugleich ein Beitrag zur Appendicitisfrage und der ihrer Bezielung zur Oxyuris. *Berlin klin. Wchnschr.*, 51: 1211, 1271, 1914.
  17. RHEINDORF, A. Beitrag zur Frage der Bedeutung der Oxyuren bei der Wurmfortsatzenzundung der Kinder. *Berlin klin. Wchnschr.*, 49: 451-503, 1917.
  18. CECIL, R. L., and BUCKLEY, K. On the lesions produced in the appendix by oxyuris vermicularis and trichocephalus trichiura. *J. Exper. Med.*, 15: 225-245, 1912.
  19. RIFF, A. Contribution à l'étiologie de l'appendicite. *Presse méd.*, 27: 521-524, 1919.
  20. HARRIS, W. H., and BROWNE, D. C. Oxyuris vermicularis as a causative factor in appendicitis. *J. A. M. A.*, 84: 650-654, 1925.
  21. INNES, J. A., and CAMPBELL, A. E. The occurrence of oxyuris vermicularis in the human vermiform appendix. *Parasitology*, 7: 189-200, 1914-1915.
  22. ASCHOFF, A. Appendicopathia oxyurica (Pseudo-appendicitis ex oxyure). *Med. klin.*, 9: 249-251, 1913.
  23. ASCHOFF, A. Sind die Würmer, besonders die Oxyuren, direkt oder indirekt schuld an der Appendicitis? *Berlin klin. Wchnschr.*, 51: 1504-1507, 1914.
  24. ASCHOFF, A. Müssen wir unsere Anschauungen über die Aetiologie der Wurmfortsätzentzündung ändern? *Berlin klin. Wchnschr.*, 57: 1041-1046, 1920.
  25. HUECK, O. Ueber die pathologische Bedeutung von Helminthen in der appendix. *Frankfurt. Ztschr. f. Path.*, 13: 434-474, 1913.
  26. BRAUCH, M. Ueber Appendicopathia oxyurica. *Beitr. z. Path. Anat. u. z. allg. Path.*, 71: 207, 262, 1922.
  27. DRIGALSKI, W., and KOCK, E. W. Ueber die Bedeutung des Wurmfortsatzes für die Entwicklung der Oxyuren. *Deutsche med. Wchnschr.*, 51: 309-311, 1925.
  28. STEICHELE, H. Appendicitis und Oxyuren. *Arch. f. klin. Chir.*, 135: 373-381, 1925.
  29. JAROSCHKA, K. Ueber Typhlitis und Appendicitis verursacht durch Oxyuren. *Deutsche Ztschr. f. Chir.*, 183: 99-113, 1923.
  30. SSOLOWJEW, N. J. Beiträge zur Frage ueber die Rolle der Oxyuren in der Aetiologie der Appendicitis. *Mitt. a.d. Grenzgeb. d. Med. u Chir.*, 41: 20-31, 1928.
  31. WARTHIN. Cited by Gordon.<sup>8</sup>





# TREATMENT OF VARICOSE VEINS\*

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THE injection treatment of varicose veins has enjoyed a wave of popularity in the past few years and as a result surgical procedures have fallen into discard. This is largely due to the fact that the sclerosing solutions have become more efficient, the injection treatment seemed to be less formidable than surgery, and hospitalization could be avoided. The test of time has shown that permanent results were not being obtained and more radical measures than the injection of sclerosing solutions are required for permanent relief. The treatment of varicose veins by ligation and injection is known to have been performed over thirty years ago. This form of therapy, however, was not emphasized until recently and is now recognized as the most reliable method of obtaining permanent cures.<sup>1,2,3,4</sup> There are some cases which respond to injection treatment alone, but these are in the minority. Varicosities generally are still being under-treated. Modern treatment should be more thorough treatment, with fewer recurrences.

To treat successfully varicose veins and their complications the extent of the underlying disease must be recognized. No form of therapy should be instituted until the efficiency of the valves of the saphenous and communicating veins and the patency of the deep circulation is known and arterial disease of the lower extremities ruled out. These factors are determined as follows:

A. *Tests to Determine the Valvular Competence of the Saphenous Veins and Its Communicating Branches with the Deep Circulation.* 1. Schwartz test:<sup>5</sup> The flat portions of the fingers of one hand are placed along the usual course of the saphenous vein in the thigh, and the vein is sharply tapped on one of its varicosities

below the knee. If there is incompetency of the saphenous valves, a distinct impulse is transmitted to the palpating fingers through the tense column of blood. This test is also of value in tracing the course of the saphenous vein.

2. Trendelenburg test:<sup>6</sup> This test gives information regarding competence of the valves of the saphenous and communicating veins. The affected extremity is elevated so that it is emptied of its venous blood, then rapidly lowered. If the varicosities are observed to fill rapidly, it is evidence that the valves of the saphenous vein are incompetent. The leg is again elevated, a tourniquet is placed at the saphenous femoral junction, and the leg is lowered. (Fig. 2.) If the veins of the lower leg remain collapsed or fill slowly from below it is proof that the saphenous valves are incompetent. If the varices rapidly fill, the valves of both the communicating veins and the saphenous vein are inadequate; this is a "double positive" test. (Fig. 3.)

B. *Tests to Determine the Patency of the Deep Circulation.* 1. Perthes' test:<sup>7</sup> The saphenous vein is constricted in the lower portion of the thigh and the patient is instructed to stand and flex and extend the knee vigorously ten times. If the deep circulation is functioning normally, the blood is sucked from the varicosities (superficial circulation) into the deep veins by the muscular contractions. On releasing the constriction the varicosities refill from above, demonstrating the amount of blood taken by the deep venous system.

2. Compression test: It is difficult in some individuals to evaluate the Perthes' test. In these cases the compression test is of value and may be accomplished in two ways.

\* From the Thomas-Davis Clinic.

(a) An ace bandage or an elastic stocking extending from the toes to the knee is worn by the patient for three to four days.

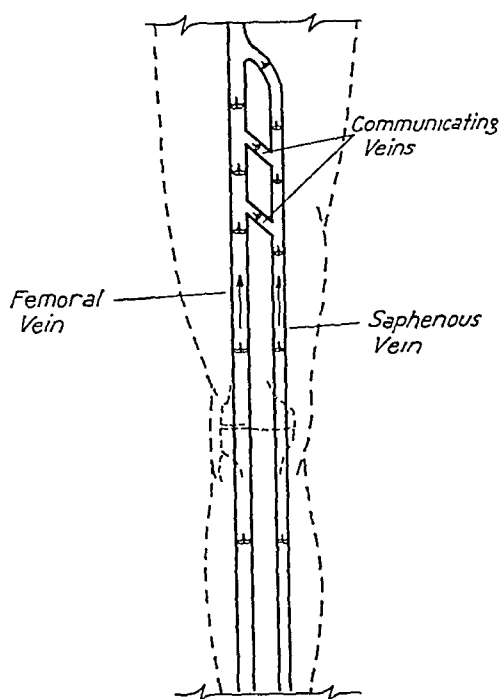


FIG. 1. Normal deep and superficial circulation with the communicating veins illustrated. Direction of blood flow indicated by arrows. Varicosities occurring with a normal valvular system such as the above should be treated by injection only. Communicating veins of lower leg not illustrated.

If his symptoms are relieved and the elastic support does not cause pain or cramping after being worn constantly, one may be assured that in all probability the deep circulation is adequate. This type of appliance compresses the superficial veins and the deep venous network must carry the venous blood.

(b) A rubber bandage is applied with enough compression to close the external veins. This should extend from the toes to above the knee with the patient lying down. The compression is maintained for forty-five to sixty minutes. If this is comfortably tolerated and there is no edema of the toes, one may be reasonably sure that the deep veins are capable of carrying on the circulation. This test should be carried out where the patient can be observed at frequent intervals and the

bandage removed if pain or discomfort of the legs or edema of the toes occurs. A past history of "milk leg" or persistent edema

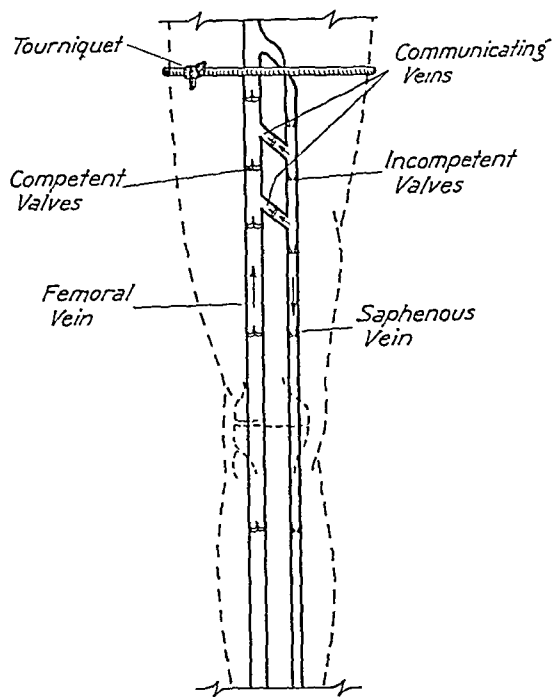


FIG. 2. Tourniquet in place for performing the Trendelenburg test. Arrows point direction of blood flow without tourniquet. Since the back flow of blood through the saphenous vein is prevented by occluding the saphenofemoral junction and communicating valves are competent, the varicosities of the lower leg slowly fill or remain collapsed when the leg is lowered. Ligation and injection of the saphenous vein are required for the cure.

of the affected extremity usually contra-indicates active treatment. If there is any doubt as to the patency of the deep circulation after performing the above tests only palliative treatment is indicated.

*C. Determining the Presence of Arterial Disease.* Arterial diseases of the lower extremities should always be ruled out before treatment is undertaken. Senile or diabetic arteriosclerosis may be detected by absence of the pulsation of the posterior tibial and dorsalis pedis arteris. Thromboangiitis obliterans is discovered, by the Samuel test where the legs are elevated to right angles to the body with the patient in the reclining position. The feet are rapidly extended and flexed. If the plantar surfaces of the feet become blanched and

pain occurs in the calf of the leg, arterial disease of the lower leg may be assumed to be present.

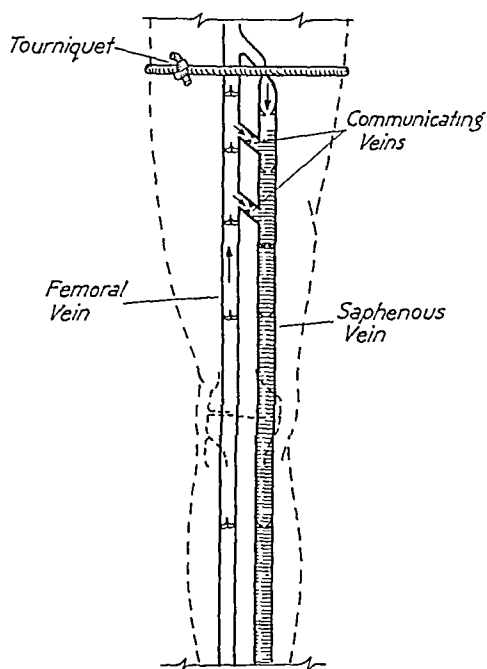


FIG. 3. Due to incompetency of the communicating as well as the saphenous valves, the varicosities rapidly fill as the tourniquet does not prevent the back flow of blood through the communicating veins. When this occurs it is a "double positive Trendelenburg test." Ligation and injection are required in these cases for permanent relief.

#### TREATMENT

1. Age, debility and prejudice against surgical procedures make it necessary to give only palliative treatment in some instances. In these cases the varices may be controlled by an elastic support of the lower extremities. These supports compress the external circulation relieving venous hydrostatic pressure. Ace bandages or elastic stockings serve this purpose well.

2. If the valves of the communicating and saphenous veins have been shown to be competent and the deep circulation patent, the varicosities may be injected at intervals, and ligation is not recommended. (Fig. 1.)

3. It has been recommended that patients with inadequate saphenous valvular systems but with normal valves of the communicating veins have ligations only at the saphenofemoral junction. We feel that

the routine ligation of the saphenous vein just above the knee immediately before ligating and injecting at the saphenofemoral junction gives the most satisfactory results, whether the communicating valves are competent or not. (Figs. 2 and 3.) In the majority of our cases we have made a third ligation between these two points injecting the distal end of the vein in the middle and upper areas. In this way the chances of the vein recanalizing are more remote and there is a more even distribution of the sclerosing solution. Lowenberg<sup>8</sup> regularly ligates the saphenous vein at the knee and in the groin since he believes that it lessens the postoperative reaction.

4. Untreated varicosities lead to complications. Of these ulceration is the most outstanding and resistant to treatment. Prolonged passive congestion results in a malnutrition of the skin, lowering its resistance so that slight trauma or infection may result in a break in its continuity. Once broken, the skin is soon infected, and an ulcer results. The skin edges of these ulcers tend constantly to separate<sup>9</sup> resulting in a wider bed for infection and more tissue destruction. Staphylococcus, streptococcus, bacillus pyocyaneus, and fungi are usually found in this type of ulcer. Consequently, both germicides and fungicides are needed for its treatment.

The conservative treatment for ulcers is to place the patient in bed with the affected extremity elevated, and apply chlorazene, diachloramine T, or mercurial compounds to the ulcer constantly. An elastic support is placed over the lower leg extending from the toes to above the knee. Healing usually takes place in two to six weeks.

This treatment is not satisfactory, and ulcers commonly recur since the varicosities, their underlying cause, have not been cared for.

Most ulcers can be cured while the patient remains ambulatory, and for economic reasons it is obviously the desired form of treatment. If the ulcer is severely infected, hot packs, elevation of the extremity, and wearing of an elastic sup-

port should be the method of treatment until the infection is under control. When the inflammation has subsided ligation of the saphenous vein is performed in the same manner as in uncomplicated cases of varices with valvular incompetence. Later the varicosities proximal to the ulcer are sclerosed by injection. The ulcer is covered with an antiseptic dye or ointment as gentian violet or merthiolate ointment. Strips of adhesive tape are placed over the ulcer, a rubber sponge is applied evenly over the adhesive and is held in place by an elastic bandage which envelopes the lower leg. The dressing should be changed every three to seven days, and if necessary, further injections can be given at the time of the dressings.

Ulcers which have persisted over a long period of time occasionally will not heal because of fibrosis and scar formation. The treatment of these ulcers must be radical, and they are cured by diminishing the infection, excising the ulcer with its scar tissue, and applying split skin grafts over the resulting raw surface.<sup>10</sup>

The most common complication of varicose veins is thrombophlebitis, which occurs in about one-half of all the patients with this condition.<sup>11</sup> Phlebitis of the saphenous vein produces palpable and visible red streaks along the vein, is usually painful, causes but little systemic reaction, and is seldom a fatal condition. The treatment of phlebitis of varicose veins varies greatly from the treatment of phlebitis of the deep circulation. Thrombophlebitis of the saphenous veins is treated actively<sup>12</sup> to prevent further extension of the thrombosis and possible embolism. Ligation and section of the saphenous vein at the saphenofemoral junction, followed later by the injection of the varicosities, is the treatment of choice. Since thrombosed veins will recanalize with loss of the venous valves,<sup>13</sup> the ligation serves two purposes: it cures the thrombophlebitis and prevents the reformation of varicose veins. Edwards<sup>11</sup> states that this "treatment is based on the attitude that the phlebitis

is but a complication, and the treatment is immediately directed against the varices." Most individuals can remain ambulatory after ligation with the support of an elastic bandage. If for any reason the patient is confined to bed, he should carry out routine exercises of the legs and move frequently. While the leg is at rest it should be elevated to promote venous circulation.

Rupture of a varix is not a major complication. Thin walled, sacculated veins rupture near the skin surface, and pressure over the site of the rupture with elevation of the leg promotes healing.

5. Few patients require second operation. Due to incompetent perforating veins in the lower leg or inadequate valves of the short saphenous vein a small number of varices do not remain closed following the ligation and injection. The operation advocated by Linton<sup>14</sup> is advised in the former and ligation of the saphenous vein in the popliteal space in the latter.

#### TECHNIQUE OF TREATMENT

1. *Injection Technique.* Before any attempt is made to produce an obliteration of a varix by injection the contraindications to this form of therapy should be ruled out. Systemic diseases, infirmity, hyperthyroidism, general or local infection, impairment of the deep or arterial circulation are all contraindications; and injection should not be done until such conditions have been corrected or cured.

Thus far no ideal sclerosing solution has been found; each has some undesirable features. A few which have proved satisfactory are 5 per cent sodium morrhuate, dextrose 50 per cent, potassium oleate 5 per cent, and monolate. We are now using this latter solution exclusively. All these substances are toxic to some degree depending upon the sensitivity of the patient and dosage. Severe reactions have been reported following the injection of some of these solutions<sup>14</sup> and large doses must not be given.

The varicosities to be injected are located by having the patient stand and

marking areas where injections are to be made with antiseptic dye such as gentian violet or mercurochrome. The patient lies down and the veins are distended by placing a tourniquet just above the knee. A 24 or 25 gauge needle is inserted into the vein at the marked area, and the tourniquet is released. The blood is stripped from this segment of the vein and the necessary amount of sclerosing solution is slowly injected through the needle. Sterile gauze is placed over this area supported by an ace bandage which is worn continuously during the period of treatment. Injections may be repeated twice weekly, using alternate legs. Two to five veins may be injected at a time, the number depending upon the amount of reaction the patient manifests.

2. *Ligation and Section of the Saphenous Vein.* A. Saphenofemoral Junction. Palpation of the femoral artery locates the saphenous vein, as the saphenofemoral junction is about 2 cm. medial to the femoral artery and 2 cm. below Poupart's ligament. With aseptic technique a local anesthetic is injected and an incision about 2 inches long made over the saphenous vein parallel to Poupart's ligament. The saphenous vein lies underneath the superficial fascia and the latter must be divided and retracted before the vein can be found resting in fatty tissue. The saphenofemoral junction is exposed with the several tributaries of the saphenous vein. The tributaries of the vein are tied and the vein itself is dissected free to its junction with the femoral vein. It is then doubly ligated so that about 1 inch of the vein can be removed between the ligatures. Each end of the vein is transfixed, using No. 1 chromic catgut suture. The distal segment of the vein is injected with the selected sclerosing agent and the wound is closed. A pressure dressing is applied and the patient is encouraged to walk as soon as he desires. If any varicosities remain they may be injected, beginning one week following the ligation and the section.

B. Lower Portion of the Vein below Its Communicating Branches. The saphenous

vein in this area lies along the posterior border of the medial condyle and may be found by making a transverse incision at this point. There are a few superficial veins which may be mistaken for the saphenous. The latter lies under the superficial fascia, however, and if this fact is kept in mind error will not occur.

C. Medial Portion between Upper and Lower Ligations. The saphenous vein is located in this area by having the patient stand before the leg is prepared for surgery. It can be found by the Schwartz test. The vein site is marked with an indelible pencil and ligation and injection are easily accomplished by the above technique.

#### REFERENCES

1. OCHSNER, A., and MAHORNER, H. R. The modern treatment of varicose veins. *Surgery*, 2: 889, 1937.
2. LEVENSON, W. S. High ligation in the treatment of varicose veins. *New England J. Med.*, 213: 972, 1935.
3. SARMA, P. J. Saphenous vein ligation. *S. Clin. North America*, P. 129 (Feb.) 1938.
4. VEAL, J. R., and VAN WERDEN, B. D. The physiologic bases for ligation of the great saphenous vein in the treatment of varicose veins. *Am. J. Surg.*, 40: 426, 1938.
5. HOMANS, J. Textbook of Surgery. Springfield, 1932. C. C. Thomas.
6. TRENDLENBERG, F. Ueber die Unterbindung der Vena saphena magna bei Unterschenkelvaricen. *Beitr. z. klin. Chir.*, 7: 195, 1891.
7. PERTHES, G. Ueber die Operation der Unterschenkelvaricen nach Trendelenberg. *Deutsche med. Wchnschr.*, 1: 253, 1895.
8. LOWENBERG, E. L. Varicose veins treated by combined ligation and injection. *Surgery*, 2: 903, 1937.
9. WHITNEY, E. T., and CONSALES, P. A. The treatment of the varicose ulcer. *New England J. Med.*, 213: 967, 1935.
10. BROWN, J. B., BYARS, L. T., and BLAIR, V. P. Study of ulcerations of lower extremities and their repair with thick split skin grafts. *Surg., Gynec. & Obst.*, 63: 273, 1936.
11. EDWARDS, E. A. Thrombophlebitis of varicose veins. *Surg., Gynec. & Obst.*, 66: 236, 1938.
12. WHITNEY, E. T. Treatment of phlebitis. *New England J. Med.*, 213: 970, 1935.
13. EDWARDS, E. A., and EDWARDS, J. E. Effect of thrombophlebitis on venous valve. *Surg., Gynec. & Obst.*, 65: 310, 1937.
14. LINTON, R. R. Communicating veins of the lower leg and the operative technic for their ligation. *Ann. Surg.*, 107: 582, 1938.
15. TRAUB, E. F., and SWARTS, W. B. Collapse complicating varicose vein injection of sodium morrhuate. *New York State J. Med.*, 37: 1506, 1937.

# CASE REPORTS

## MALIGNANT HICCUP\*†

WITH REPORT OF A CASE FOLLOWING TRANSURETHRAL PROSTATIC RESECTION  
AND REQUIRING BILATERAL PHRENICECTOMY FOR CURE

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PERSISTENT hiccup often threatens life by exhaustion; this severe variety is entitled to the designation malignant. Hiccup or singultus is produced by an intermittent spastic contraction of the diaphragm causing inspiration which is followed by a sudden closure of the glottis. The motor impulse in the usual hiccup travels over the phrenic nerve which arises at the third and fourth cervical spinal cord levels and is the most important branch of the cervical plexus. Occasionally clonic contraction of the accessory muscles of respiration (intercostal, abdominal) assists in producing hiccup and even may produce hiccup following bilateral phrenicectomy, especially in cases of central nervous system origin.<sup>1</sup> It is evident that the same muscles which function to produce hiccup operate also in vomiting but with different action. Thus sensory impulses carried by vagus fibers from irritant lesions of the larynx and other structures correspondingly innervated, may reflexly cause hiccup.<sup>2</sup>

An extensive study of the literature suggests that the clinico-therapeutic course of the patient herewith reported is unique. In a 76 year old man prolonged hiccup complicated recovery from an otherwise uneventful transurethral resection of an adenomatous prostate gland. The hiccup not only failed to respond to the more rigorous types of non-surgical treatment but finally required bilateral removal of the

phrenic nerves (phrenicectomy) to prevent death from exhaustion. A briefly detailed report of the clinical course and the varied therapy employed indicates (1) methods of treatment of hiccup and some of the potential therapeutic difficulties to be encountered; (2) the severe physical depletion persistent hiccup may induce and (3) the likely ultimate desperation of patient and physician alike. It will be noted that during an eight day period, this old gentleman suffered thirty-nine separate attacks of severe hiccup, even during sleep; the longest continuous spell was twenty-one and a half hours.

### CASE REPORT

F. S., a retired teacher, 76 years of age, presented himself October 18, 1934 because of difficulty and frequency of urination of gradually increasing severity during the previous fifteen years. During the day he urinated every two hours, he voided two to three times nightly, suffered some urgency with periodic hesitancy, occasionally urinary dribbling and perineal pain. Ten years previously he had hiccupped intermittently for several days following inguinal hernioplasty.

Urologic examination disclosed 2 ounces of residual urine; the voided urine was clear, the specific gravity was 1.022, albumin graded one plus was found, and an occasional leucocyte. By rectum the prostate felt twice normal size and was smoothly elastic. Cystoscopy revealed a moderate adenomatous hypertrophy of the

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median prostatic lobe. Lateral prostatic lobe hypertrophy was graded two plus; hypertrophy of the trigone and moderate generalized trabeculation of the bladder wall completed the cystoscopic picture.

On October 24 the patient was sent to Mountainside Hospital. The nonprotein nitrogen was determined to be 31.59 mg. per 100 c.c. of blood and the CO<sub>2</sub> plasma combining power 56 volumes per cent.

On October 25 under low spinal anesthesia bilateral vasectomy and transurethral prostatic resection were performed. The middle prostatic lobe and the adjacent lower segments of the lateral lobes were generously excised; the removed tissue was not weighed. There was slight bleeding; a 24 F. catheter was left indwelling.

The patient was returned to his bed where he was given an intravenous infusion of 1300 c. c. of normal saline. In the afternoon 500 c. c. of normal saline and 500 c. c. of 10 per cent glucose were given intravenously. During the day the patient excreted 450 c. c. of urine. That night he vomited 150 c. c. of fluids and the following morning complained of gas pains which were partially relieved by a flaxseed poultice and rectal tube. In the afternoon of the first day postoperative, 1500 c. c. of normal saline-5 per cent glucose was again given hypodermically and flaxseed poultices together with an inlying rectal tube were again employed because of moderate abdominal distention. That night (second postoperative) there was emesis of small amounts of bile stained fluid, but this was temporarily checked by an opium derivative (pantopon) hypodermically.

The following morning, forty-four hours postoperative, the patient hiccupped for fifteen minutes and from this point, the complicating hiccup and its treatment can most briefly be recorded in a tabular manner. During the eight day period of exhausting hiccupping the fluid intake (chiefly intravenous) varied between 2,430 and 3,470 c. c. in twenty-four hours. Also not indicated in the tabulation of hiccup was the diligent and almost exhausting use of of the commonly employed procedures to combat abdominal distention. This included enemas (soapsuds, soda bicarbonate, milk and molasses), pitressin hypodermically, hot abdominal poultices, inlying rectal tube, gastric lavage and inlying Levine gastric tube. Stimulation was often necessary; caffeine sodium

Date	Hour	Event	Treatment
10/25	11 A M	Prostatic resection	
10/27 (Second postop day)	7 50 A M	Hiccup began, 15 minutes	Deep breathing and blowing into paper bag (rebreathing) No result 98 per cent CO <sub>2</sub> breathing through anesthesia respirator for three minutes
	8 15 A M	Hiccup stopped	
	10 45 A M	Hiccupping	CO <sub>2</sub> breathing for five minutes without effect
	12 30 P M	Hiccupping	CO <sub>2</sub> breathing for five minutes without effect
	1 40 P M	Hiccupping stopped	Flaxseed poultice with rectal tube
	1 50 P M	Hiccup resumed	Inhalation of pure oxygen No effect Blood pressure 128/60 mm Hg Inhalation CO <sub>2</sub>
	3 05 P M		
	3 10 P M	Hiccup stopped	
	4 15 P M	Hiccup resumed	CO <sub>2</sub> rebreathing five minutes
	4 20 P M	Hiccup stopped	
	5 P M	Hiccup resumed	
	7 45 P M	Hiccupping and distention	Levine tube passed and fastened in situ, connected with continuous suction drainage Hiccup stopped for forty-five minutes
	8 30 P M	Hiccup resumed, weakness	Levine tube removed Caffeine sodium benzoate gr 5
	11 P M	Hiccup stopped	
	12 P M	Hiccup resumed	Sodium pentobarbital gr 1½
10/28 (Third postop day)	12 30 A M	Hiccup stopped	
	3 A M	Hiccup resumed	CO <sub>2</sub> and oxygen for fifteen minutes Pantopon gr ¼, hypo
	4 A M		
	4 15 A M	Hiccup stopped while sleeping	
	5 A M	Hiccup resumed	
	7 A M	More cheerful, abdomen soft, complaining of "acid stomach"	
	7 A M	Hiccup ceased	
	8 A M	Hiccup resumed	Pitressin 1 ampule Uvula painted with tincture of iodine
	9 A M		
	9 05 A M	Hiccup stopped	
	9 10 A M	Hiccup resumed	Rhubarb and soda 2 drams no effect Blowing into paper bag no effect Blowing into empty-ema blow bottles Hiccup stopped after twenty-five minutes of this
	10 45 A M		
	11 10 A M	Hiccup stopped	
	12 30 P M	Hiccup resumed	Use of blow bottles was ineffective, but patient stopped hiccupping some time later
	1 P M	Hiccup stopped	
	4 30 P M	Hiccup resumed	
	6 30 P M	Hiccup ceased	
	6 35 P M	Hiccup resumed	Blow bottles used but hiccup occurred in a few minutes

Date	Hour	Event	Treatment	Date	Hour	Event	Treatment
10/29 (Fourth postop day)	9 P M		Sodium pentobarbital gr $1\frac{1}{2}$		7 20 P M	Hiccup stopped	
	9 15 P M	Hiccup stopped			8 20 P M	Hiccup resumed	
	10 30 P M	Hiccup resumed			8 40 P M		Atropine sulfate gr $\frac{1}{50}$ Surgical ether anesthesia
	11 30 P M		Pantopon gr $\frac{1}{3}$				
	4 A M		Pantopon gr $\frac{1}{3}$	10/31 (Sixth postop day)	10 45 P M	Hiccup stopped	
			Patient slept about ninety minutes after narcotic but hiccup continued		12 30 A M	Hiccup resumed	
			Pitressin, 1 ampule		1 30 A M		Atropine sulfate gr $\frac{1}{50}$
	8 A M	Abdominal distention			3 30 A M		Inhalation of CO <sub>2</sub> for thirty minutes
	9 A M	Still hiccupping	Levine tube reinserted Magnesium sulfate 2 ounces through tube		10 A M	Hiccup continued	Indwelling catheter removed Atropine sulfate gr $\frac{1}{100}$
	10 A M	Hiccupping	Mustard paste to anterior chest for fifteen minutes		12 M		Diathermy to posterior chest
	12 30 P M		Tincture of benzoin inhalations		1 00 P M	Hiccup ceased	Atropine sulfate gr $\frac{1}{100}$
	12 40 P M	Hiccup stopped	98 per cent CO <sub>2</sub> breathing		2 00 P M	Hiccup resumed	Infusion 2,250 c c saline 5 per cent glucose intravenously, containing 15 ounces of 10 per cent novocaine
	1 20 P M	Hiccup resumed	98 per cent CO <sub>2</sub> breathing No effect				Diathermy to posterior chest
	2 P M		Morphine sulfate gr $\frac{1}{4}$		2 30 P M		Atropine sulfate gr $\frac{1}{100}$ Patient sleeping at long intervals but still hiccupping
	2 15 P M	Hiccupping	Mustard paste to anterior chest				
	3 30 P M	Still hiccupping	Tincture benzoin inhalations		9 P M	Still hiccupping	Calomel gr 3, soda bicarbonate gr 10, benzyl benzoate drams 2 in 4 ounces water and 2 drams sugar
	4 P M		Oil of cayeput 2 minims in 1 teaspoonful of sugar				
	4 30 P M	Hiccupping stopped	Pitressin, 1 ampule		12 30 A M		Hyoscine hydrobromide gr $\frac{1}{50}$ , morphine sulfate gr $\frac{1}{3}$ , caffeine sodium benzoate gr 2 by hypodermic
	5 P M	Hiccup resumed		11/1 (Seventh postop day)	12 35 A M		Surgical chloroform anesthesia (5 ounces)
	5 45 P M				12 45 A M	Hiccup ceased	
10/30 (Fifth postop day)	6 40 P M	Hiccup continued	Mustard paste to anterior chest, tincture of benzoin inhalations		1 A M		Avertin rectal anesthesia
			Very weak Hypodermic hyoscine hydrobromide gr $\frac{1}{100}$ , morphine sulfate gr $\frac{1}{6}$ , caffeine sodium benzoate gr 2		3 30 A M	Hiccup resumed	Avertin rectal anesthesia
	2 30 A M		Sodium pentobarbital gr $1\frac{1}{2}$ Pantopon gr $\frac{1}{3}$ Still hiccupping though sleeping for two hours		6 30 A M	Hiccup continued	Benzyl benzoate 2 drams with 2 drams sugar in 4 ounces water
	3 30 A M		98 per cent CO <sub>2</sub> rebreathing for five minutes Hiccup continued		9 A M		Sodium bicarbonate enema followed by turpentine stupes and later by tight abdominal binder
	8 A M		Pitressin, 1 ampule		10 A M		Sodium amytal gr 3 Periodically irrational, incontinent
	12 A M		Avertin rectal anesthesia profound		10 40 A M		
	2 30 P M		Hiccup continued		11 A M	Hiccup stopped	
	2 35 P M	Hiccup stopped	Oil of cayeput minims 2 on 1 teaspoonful sugar		11 10 A M	Hiccup resumed	
	2 40 P M	Hiccup resumed			11 30 A M		Hypodermoclysis of normal saline—5 per cent glucose 2,250 c c and $1\frac{1}{2}$ ounces 10 per cent novocaine
	4 45 P M		5 minims chloroform in 1 dram aromatic elixir Depressed, crying, spitting blood				Sodium amytal gr 3 Abdominal belt tightened
	6 30 P M		5 minims chloroform in 1 dram aromatic elixir		11 40 A M		Sodium bromide gr 60, chloral hydrate gr 25, by rectum
	7 10 P M	Hiccupping	Atropine sulfate gr $\frac{1}{100}$ Tincture benzoin inhalation		1 10 P M	Hiccup continued	
			Shallow breathing				



Date	Hour	Event	Treatment
11/2 (Eighth postop day)	3 30 P M		Expelled thirty minutes later Sodium amytal gr 3 Snoring noisily but still hiccuping
	4 15 P M	Hiccup ceased	
	4 50 P M	Hiccup resumed	
	6 P M	Hiccup ceased	
	8 15 P M	Hiccup resumed	Turpentine abdominal stupes Patient sleeping, confused, irrational at times
	9 P M		Sodium amytal gr 3 Hiccup continued
	11 45 P M	Hiccup ceased	
	12 20 A M	Hiccup resumed	
	12 40 A M		Abdominal belt replaced Sodium amytal gr 3
	1 15 A M	Hiccup stopped	
	1 45 A M	Hiccup resumed	
	7 40 A M	Hiccup ceased	
	8 30 A M	Hiccup resumed	
	9 A M		CO <sub>2</sub> estimation 58 volumes per cent and NPN 31 59 mg per 100 c.c. of blood
	10 30 A M	Hiccup continued	Sodium amytal gr 3
	10 45 A M	Hiccup ceased	
	12 55 P M	..	Sodium amytal gr 3
	1 40 P M		Saturated alcoholic solution of menthol 10 minims
	2 40 P M		Saturated alcoholic solution of menthol 10 minims
	3 40 P M		Saturated alcoholic solution of menthol 10 minims
	3 45 P M	Hiccup resumed	
	4 40 P M		Saturated alcoholic solution of menthol 10 minims
	5 P M		Saturated alcoholic solution of menthol 10 minims Whiskey drams 2 in eggnog
	9 30 P M	Hiccup continued	Chloral hydrate gr 40, triple bromides gr 60 by rectum Sodium amytal gr 3
	10 30 P M		
	11 45 P M	Hiccup ceased	
	12 15 A M	Hiccup resumed	
11/3 (Ninth postop day)	2 45 A M		Sodium amytal gr 3
	3 30 A M	Hiccup ceased	
	4 30 A M	Hiccup resumed	
	7 A M	Hiccup ceased	
	9 30 A M	Hiccup resumed	Restless, disoriented
	10 15 A M		Morphine sulfate gr 1/4, atropine sulfate gr 1/100
	2 P M	Hiccup ceased	
	4 P M	Hiccup resumed	
	5 P M	Hiccup ceased	
	5 15 P M	Hiccup resumed	
7 50 P M Operation (by the late Dr Pol Coryllos, called in consultation) Novocaine (1 per cent) injection and crushing of left phrenic nerve, the left side of the diaphragm appearing to be the pacemaker. Branches to the fourth cervical root (two), subclavius muscle (one), and scalenus muscle (one) were cut. Hiccup temporarily stopped soon after injection of			

Date	Hour	Event	Treatment
11/4 (Tenth postop day)		novocaine into the deep cervical fascia Before crushing the nerve, its identity was verified by contraction of the diaphragm produced by clamping the nerve Following left phrenicectomy, the left pupil became larger than the right	
	9 30 P M	Hiccup resumed	
	10 P M		Morphine sulfate gr 1/4, atropine sulfate gr 1/100 Oratol gr 3
	10 45 P M		
	10 50 P M	Hiccup ceased	
	1 40 A M	Hiccup resumed	
	3 40 A M		Morphine sulfate gr 1/4, atropine sulfate gr 1/100
	6 10 A M	Hiccup ceased	
	7 45 A M	Hiccup resumed	
	8 45 A M	Hiccup ceased	
	9 15 A M	Hiccup resumed	
	12 30 P M	Operation, bilateral phrenicectomy (Dr Pol Coryllos) Cutting of all visible ramus and crushing of right phrenic nerve scarcely influenced the hiccup, therefore evulsion was decided upon and the nerve, 12 inches long, was removed. Hiccup persisted. The left operative wound of the day previous was reopened and the phrenic nerve (13 inches) was evulsed. It was only when 3 inches of the nerve had been pulled out by rolling on a clamp that the hiccup stopped. Following evulsion, hiccup stopped permanently	

benzoate was employed. An ineffective effort was made to maintain nutrition by the administration of readily digestible foodstuffs of high caloric value.

From this point the convalescence was that of a greatly debilitated aged patient. An electrocardiographic study on November 5 was considered normal. Examination of the chest showed a mild consolidation (dullness, bronchial breathing, egophony, pectoriloquy) of the left lower lobe posteriorly. Fluoroscopic examination revealed marked elevation of the diaphragm coincident to atonic relaxation. The patient continued to have moderate post-operative irritability of the vesical outlet and posterior urethra. Blow bottles were employed for a few minutes every hour during which the patient was awake. The temperature curve ranged between 99°F. and 101 except on the ninth day and immediately following bilateral phrenicectomy on which occasion it reached 102.6°F. Thereafter it promptly became normal and remained so until the patient was discharged from the hospital. He was able to sit on the edge of his bed November 11 and was out of bed two days later, returning home on November 24, exactly one month after entering the hospital.

Since leaving the hospital he has been about regularly, attends to household chores and the furnace, shovels snow, works in his garden, goes to camp in the summer and performs other activities of which few men of his years are

capable. He has a slight dyspnea on exertion; he exhibits paradoxical breathing (abdominal relaxation and protrusion on inspiration) and still complains of some urinary frequency. When examined urologically one year ago his urine showed scattered leucocytes; rectal examination disclosed no important prostatic change during four years and he emptied his bladder completely. Today at 81 years he is still seen on the streets, though he is, of course, in his dotage.

#### DISCUSSION

Hiccup is a neuromuscular reflex mechanism and may be caused by any irritation (1) of the afferent pathway to the phrenic nerve centers in the upper cervical cord, (2) of the cord and central centers themselves, or (3) of the efferent pathways to the muscles whose clonic contraction produces hiccup. Examples of these etiologic groups are indicated in the following:

1. *Afferent Nerve Irritation.* Gastrointestinal tract: Swallowing of irritating or hot fluid or food, esophageal or gastric lesions (esophagitis, gastritis, gastric distention), bowel distention, obstruction, ileus, strangulated hernia, acute appendicitis, typhoid, acute pancreatitis, acute biliary and hepatic lesions, peritonitis.

Pulmonary tract: laryngitis, bronchitis, pneumonia, tumors, empyema, pleurisy, phrenic and subphrenic inflammation and abscesses. As noted in the introductory paragraph, hiccup and vomiting are produced by contraction of the same muscles and any lesion which induces irritation of vagus sensory filaments may reflexly cause hiccup.

Mediastinal lesions: inflammations, adhesions, abscesses, tumors, caseous glands, cardiac enlargement, aortic aneurysm,<sup>3</sup> adhesive pericarditis. Pulmonary and mediastinal lesions may also cause hiccup through direct irritation of the phrenic nerve or of the diaphragm.

2. *Central Irritation.* Primary or metastatic cerebral or medullary tumors may directly or reflexly induce hiccup. The third and fourth cervical spinal roots may be irritated by (1) meningeal lesions such

as syphilitic meningitis, (2) cervical pachymeningitis, (3) disease of the surrounding vertebrae, such as dislocation, fracture, tumor or spondylitis. Central perineuritis may result as a centripetal extension along the phrenic nerve from pleural and diaphragmatic inflammation.

3. *Efferent Nerve Irritation.* As indicated in the second preceding paragraph, lesions of or adjacent to the phrenic nerve may be etiologic in producing hiccup.

Acute or chronic alcoholism may cause gastric irritation, toxic encephalitis or neuritis. Sulfanilamide<sup>4</sup> and serum sickness (anthrax antiserum<sup>5</sup>) have also been reported as toxic causes. Byrnes<sup>6</sup> observed crises of hiccups in tabes dorsalis. Psychogenic hiccup is occasionally observed in nervously unstable patients, may last a week or more, but always ceases during eating. My patient hiccupped during meals and sleep.

#### TREATMENT

In most instances treatment can properly be directed against the etiologic irritative factor. Yet the fact that more than 200 remedies have been advocated attests to the frequent therapeutic difficulties.

Simple and commonly employed treatment of hiccup includes physical or psychic counter-irritative methods such as firm prolonged traction of the tongue, application of an ice cap to the neck, tickling the inner nares with a feather, painting the uvula with tincture of iodine or other irritant, inhaling fumes of ether, chloroform, nitroglycerine or smelling salts, drinking cold water from the far side of a glass, drinking undiluted whiskey (1 ounce or so), Worcestershire sauce, or other gastric irritant, pressure on the phrenic nerves between the heads of the sternocleidomastoid muscles, pressure on the upper lip, eyeballs or on the ribs near the origins of the diaphragm, holding the breath as long as possible, a sudden fright, electric stimulation of the phrenic nerves, epigastrium and abdominal muscles, spraying ethyl chloride over the epigastrium

and upper abdomen, and deep diathermy to lower chest. Blowing into a paper bag (modified CO<sub>2</sub> rebreathing) is often successful in stopping hiccup and direct rebreathing of 90 per cent oxygen or of 98 per cent CO<sub>2</sub> using a regular closed anesthesia mask is even more likely to succeed. This was extensively employed with my patient. This patient also received periodically for two days a mixture of 5 minims of chloroform in 1 dram of aromatic elixir.

When postoperative or other types of gastrointestinal distention cause the hiccup, pitressin, prostigmin, hot stupes, medicated enemas, gastric lavage or intestinal decompression by periodic or continuous suction through a Levine gastric tube, may be effective. In the case reported here, postoperative gastrointestinal dysfunction and distention seem the likely explanation of the hiccup. The history of persistent though milder hiccup after herniotomy ten years before suggests a low threshold of hiccup reflex.

It is likely that in many cases of prolonged hiccup disturbances of fluid and salt balance may play an etiologic role. Dr. Max Peet, neurosurgeon to the University of Michigan Hospital writes<sup>7</sup> "I have seen a number of old men who developed hiccup after a prostatic resection, but in every instance we were able to overcome the hiccup by giving very large quantities of fluid intravenously. Usually 5000 to 6000 c.c. were given in twenty-four hours. The results in some cases were miraculous." This is a valuable therapeutic hint and had we known, we might have successfully employed it. In our case, the fluid intake was kept moderate (2,430-3,470 c.c. in twenty-four hours) simply to meet estimated fluid requirements and to prevent cardiac overloading in an aged patient. The intravenous administration of hypertonic sodium chloride solution (e.g., 50 c.c. of a 20 per cent solution) with a view to stimulation of intestinal peristalsis was considered but consensus ruled against.

Vomiting induced by the administration of apomorphine gr.  $\frac{1}{8}$  (adult) may help

to evacuate the intestinal tract and remove the irritative focus; Byrnes<sup>6</sup> suggests giving 20 gr. of zinc sulfate with the apomorphine. Hyoscine hydrobromide gr.  $\frac{1}{100}$  may afford adequate sedation. Yet morphine is best except when inflammation of the higher centers exists, as, for example, in epidemic encephalitis; in such cases spinal tap may give relief. The antispasmodic effect of benzyl benzoate (2 c.c. of 20 per cent solution) has sometimes checked hiccup. Shaine<sup>8</sup> has recently reported cessation of persistent hiccup 15 to 20 minutes following the hypodermic administration of 10 to 20 mg. of benzedrine sulfate (benzyl methyl carbinamine or beta-phenylisopropylamine sulfate) which relaxes the smooth muscle of the gastrointestinal tract. Antiluetic therapy has stopped persistent hiccup in tabes.<sup>6,9</sup> The ingestion of aromatic oils has been recommended; these include oil of peppermint (oleum menthol piperitae), oil of lavender (oleum lavendula), oil of orange (oleum aurenti), oil of ginger (oleoresina zingiberis) and as used in the case here reported oil of cajeput (oleum cajeputi).

When the primary irritative lesion cannot be identified or cannot be adequately controlled, drugs may be administered to minimize irritant sensory impulses and reflex reactions. These medications include the barbituric acid derivatives, morphine and other opium derivatives, and in severe cases, general anesthetics such as avertin, nitrous oxide, ethylene or even chloroform. In the case of the elderly patient here reported, deep surgical anesthesia induced once with ether and again with chloroform was utterly ineffective. Spinal anesthesia may successfully block the hiccup producing reflex arc in severe persistent intestinal, and particularly peritoneal irritative lesions. A tight abdominal binder will reduce somewhat the severe physical strain and fatigue consequent to the continuous muscular exertion.

When, as in our case, conservative methods of treatment fail and the condition of the patient becomes critical, injection

of one or both phrenic nerves with novocaine (1 to 5 per cent) may permanently stop the hiccup; in any event it will usually stop hiccup for two or three days. If injection fails, nerve crushing or even phrenicectomy must be resorted to. Operation on the phrenic nerve to be effective must include division of all of the filaments; anomalous radicles may be overlooked. In the case here reported the left side of the diaphragm was apparently the pacemaker, hence this phrenic nerve was attacked first.

Unilateral paralysis of the diaphragm produces no symptoms; bilateral paralysis results in dyspnea on exertion and sometimes even when the patient is at rest. Moreover, in bilateral phrenic paralysis coughing and straining at stool are often unsatisfactorily performed; chronic congestion of the base of the lungs also results. Yet the aged patient here reported suffered these handicaps to an amazingly slight degree and owes his relatively active existence to bilateral phrenicectomy.

#### SUMMARY

A case is reported of persistent hiccup requiring bilateral phrenicectomy for cure. The mechanics of the hiccup reflex mecha-

nism are discussed together with the various advocated methods of treatment. Although hiccup is usually a simple transient disturbance which readily responds to conservative treatment, persistent hiccup may seriously threaten life. In the last circumstance, phrenic nerve injection, crushing, or excision—unilateral or bilateral—is indicated and is often life saving. The phrenic nerve surgery is best entrusted to an experienced thoracic surgeon.

#### REFERENCES

1. KAPPIS, M. Origin and treatment of hiccup. *Klin. Wchnschr.*, 3: 1065, 1924.
2. GOETZ, O. *Zentralbl. f. Chir.*, 47: 1290, 1920.
3. FELIX, W. Anatomische, experimentelle und klinische Untersuchungen über den Phrenicus und über die Zwerchfellinnervation. *Deutsche Ztschr. f. Chir.*, 283: 171, 1922.
4. BERCOVICH, A., and CHAROSKY, L. Phrenicotomy in incoercible hiccup due to aortic aneurysm. *Prensa med. argent.*, 23: 2436, 1936.
5. WYMAN, M. H. Unusual reaction to sulfanilamide. *South. M. & S.*, 100: 15, 1938.
6. MIRONESCU, T., and LAZARESCU, A. Le hoquet postsérothérapique. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 52: 731, 1936.
7. BYRNES, C. M. Hiccup crises in tabes dorsalis. *Bull. Johns Hopkins Hosp.*, 56: 264, 1935.
8. PEET, M. Personal communication.
9. SHAINÉ, M. S. Benzedrine sulfate in persistent hiccup. *Am. J. M. Sc.*, 196: 715, 1938.
10. KROH, F. *München. med. Wchnschr.*, 69: 807, 1922.



# CONGENITAL MALIGNANT TUMOR OF THE SKIN IN THE NEWBORN

## REPORT OF CASE

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CONGENITAL malignant tumor of the skin in the newborn is so rarely seen that when this condition is found it may not be recognized as such. Little attention is given it until the growth has either spread or metastasized to such an extent that diagnosis offers no problem, but the outcome is usually fatal.

Reference to the literature on congenital malignant tumors in the newborn yields a dearth of reports of such cases. However, there are many reports of neoplasms other than of the skin occurring in childhood and youth. The earliest report which we have been able to find of a case of congenital malignant tumor of the skin is by Ritter<sup>1</sup> in 1864. He described a case of proliferating carcinoma of the skin over the tip of the nose in a nursling of a few months. He commented that since neither the cartilage nor the epidermis was the site of origin of the tumor, it must be assumed that the origin was in the connective tissues of the cutis. On the basis of this comment it is apparent that this was a case of sarcoma rather than carcinoma. Korte,<sup>2</sup> Bedford,<sup>3</sup> and Anzilotti<sup>4</sup> each reported single cases of congenital malignant tumor of the skin in the newborn. Bedford's case, however, was metastatic due to carcinoma of the thymus.

That congenital malignant tumors other than of the skin occurring in the newborn, though not rare, are not common is shown by the few reports in the literature. Pearl<sup>5</sup> finds that in 6,670 necropsies 12.2 per cent showed some form of malignancy but none in the newborn. Anzilotti<sup>4</sup> in his article mentions Stubiger who collected five cases. Schorr and Stahr each described single cases while Teri<sup>6</sup> reported on three cases. Dudits and Szabo,<sup>7</sup> Lain,<sup>8</sup> Colloridi,<sup>9</sup> Canavan and Hemsath,<sup>10</sup> and Frank and his

associates<sup>11</sup> reported single instances of congenital malignant tumors in the newborn. Lain, in reviewing the literature pointed out that "the periodical literature contains little on the subject of congenital cancer." He quoted Roger W. Williams as stating in 1908 "that prenatal life, infancy and childhood are completely exempt from malignant epithelial tumors" and adds "that in spite of a few exceptional cases of this kind it may be safely asserted that, under the age of puberty cancer is practically unknown."

Phillip<sup>12</sup> reviewed the literature and collected sixteen cases of non-congenital growth comprising 17 per cent of all types of malignancy. In most of these cases the growths developed on a basis of xeroderma pigmentosa; some developed spontaneously. The majority were squamous cell carcinoma. Rosner<sup>13</sup> in his statistics included 4,513 patients with cancer of the skin or natural orifices. Of these, twenty-two cases occurred between the ages of 1 and 10 years. Nothing is said about skin cancer in the newborn. Duzan<sup>14</sup> analyzed the regional distribution of 182 malignant tumors in early infancy and found none in the skin, while Picot<sup>15</sup> found only eight cases of skin cancer in 424 malignant tumors of early infancy. Dean and Pack<sup>16</sup> reported on 155 malignant tumors in patients under ten years of age at the Memorial Hospital (New York) and found only four in the skin, but they did not state whether any of these were congenital or in the newborn. They cite D'Espine and Piso who studied the regional distribution of 393 malignant tumors in children and found none in the skin. Pack and LeFevre<sup>17</sup> reported on 19,129 patients with neoplastic disease accepted for treatment at the

Memorial Hospital from January 1, 1917, to January 1, 1929. Of these tumors 16,565 were malignant. They found that 5 per cent

a full term with eutocic birth. The antenatal period had been uneventful, and there was no history of familial disease or neoplasms. At the

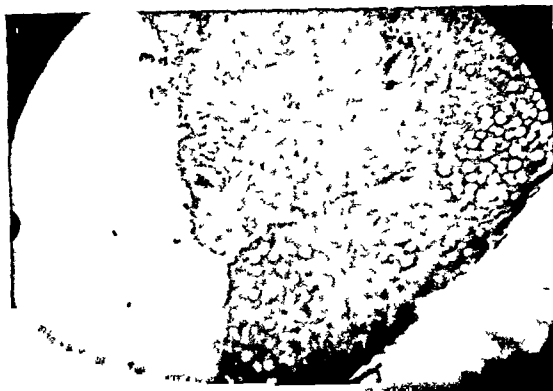


FIG. 1. Low power, showing general pattern of typical malignant tumor cells and some fat cells.

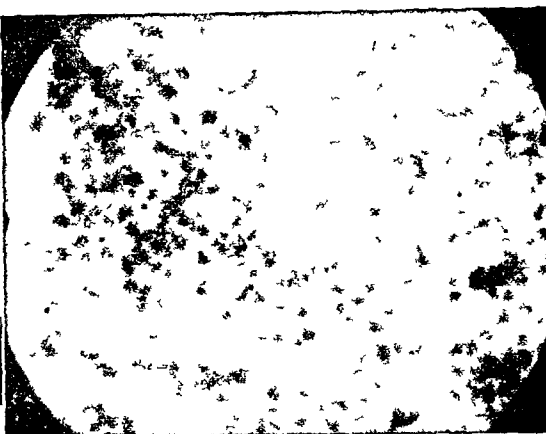


FIG. 2. High power, showing large round polyhedral cells, with densely staining nuclei, mitosis and metaplasia into fat cells.

of patients admitted to Memorial Hospital had "epidermoid carcinoma of the skin." "Only 0.64 per cent were individuals under 25 years (seven instances); of these, the youngest was a male infant 15 months, whose tumor was embryonal in character." Here, again, the rarity of congenital malignant tumor of the skin in the newborn is brought out by the fact that out of 16,565 patients with malignant tumors, there were none with malignancy of the skin in the newborn.

Cancers in youth when compared with similar tumors in mature or later life are more rapidly growing, and of greater malignancy. The history of the disease is short, the course is rapid and the mortality high. Rankin and Broders<sup>18</sup> state "that active tissue of youth, instead of resisting cancer invasion, invites its spread and the young person who is host to a malignant neoplasm has little chance for longevity, regardless of the type of therapeutic measures instituted." Pack and LeFevre<sup>17</sup> believe that "inheritance is not as important a factor in the genesis of the malignant tumors of childhood as the congenital influence of misplaced, embryonal cell rests."

#### REPORT OF CASE

S. W., male, of Jewish parentage, was born at the Methodist Hospital, August 22, 1937,

time of birth a small tumor in the skin at the left posterior axillary fold was noticed. However, the child appeared well developed, weighed 6 pounds, and cried lustily. It was examined for any abnormalities or malformations, and aside from the tumor in the left posterior axillary fold, none were found.

The tumor was pale bluish-red in color, slightly larger than a five cent piece; it was sharply demarcated in the skin, and but very slightly, if at all, elevated. The surrounding skin appeared normal in color, texture and elasticity. The tumor felt somewhat hard and resistant, and was fixed in the skin; its depth could not be determined, but it was not fixed to the underlying structures. It was apparently not painful, as pinching or pressure over the growth did not cause the baby to cry.

Two days after birth the tumor and the surrounding skin for about 3 cm. assumed an inflammatory appearance as in a localized cellulitis. The adjacent skin became red, infiltrated, warmer, and less pliable than normal. There was no fever. This condition persisted for about two days and then subsided, leaving the tumor and surrounding skin as at birth.

A circumcision was done on the eighth day in conformity to the religious rite. The wound healed normally in about five to six days. Roentgen examination of almost the complete torso of the child showed no bone changes or any other pathology.

During the next five weeks the child progressed normally, gained weight, and seemed healthy. Examination at the end of this time

showed a decided alteration in the appearance of the tumor. Its color had changed from the original pale bluish-red to a grayish yellow. The surface, which at birth was smooth and even, felt nodular. The tumor as a whole did not appear to have increased in size, nor had it become more elevated above the surrounding skin. However, the growth was definitely hard and solid, and gave the impression of being slightly fixed to the underlying tissue.

On October 5, 1937, the tumor with about 1 cm. of surrounding normal skin was excised. It was found that the growth involved the skin and subcutaneous fat down to but not involving the underlying infrapinnatus muscle. The growth easily peeled off the muscle, leaving the muscle fibers undisrupted and not bleeding. After the mass was removed the skin edges of the wound were slightly undermined to permit approximation without tension. The wound was closed, obliterating the dead space, and the skin edges brought together with three interrupted silk sutures.

The gross appearance of the tumor gave the impression of malignancy. It was solid, the cut surface gray in color with greasy, granular appearance. There was no evidence of capsulation, but rather an indefinite demarcation from the surrounding subcutaneous tissue. The growth seemed to fade irregularly into the surrounding fat.

Four days after excision the wound broke down, and a small amount of fatty, serous exudate stained the dressings. The sutures by this time were loose, and were removed, leaving the wound somewhat gaping. Although the wound was not infected, the tissue did not seem healthy, being gray in color and bathed in a small amount of greasy exudate. The wound was redressed daily with dry sterile dressings, and in about fifteen days it had filled in and closed over, leaving a small scar. About three weeks after the wound had healed there gradually appeared six small nodules, each the size of a BB shot, one at each stitch mark. These nodules were hard, slightly elevated, and of the same grayish yellow color as the original tumor just before its excision.

On November 11, 1937, a 10 mg. plaque of radium was applied over the site of the operation, covering most of the nodules, and was left in place for three and one-half hours. Due to the size of the radium plaque used all the nodules could not be covered. For the following two weeks the treated area was erythematous,

and as the erythema subsided the nodules which had been exposed to the radium gradually disappeared, leaving the skin soft, pliable and of normal appearance.

It is now more than nine months since the radium was used and there is no evidence of a recurrence. The nodules that were not treated have remained about the same size. These were likewise treated with radium.\*

Sections of the tumor were sent to some of the better-known pathologists of the country. Two were in accord as to diagnosis; the others all had different interpretations. The acting laboratory director of the Methodist Hospital, Dr. B. M. Edlavitch, reported the tissue as being a sarcoma, the exact type of which he could not differentiate. A pathologist of a large private laboratory diagnosed the tissue as "endothelial sarcoma, probably from skin or blood vessel." Another, a pathologist to a midwestern state medical university, stated that the neoplasm showed definite evidence of malignancy. Because he had never seen one like it, he said he could not positively differentiate it, but he was of the opinion that it was a fibroblastic sarcoma. Another pathologist stated that it was a relatively rare tumor composed of embryonic fat cells, numerous regular mitotic figures and large masses of eosinophiles. He diagnosed the tumor as a lipoblastoma, relatively benign, and added that it was not radiosensitive and would not be affected by radiation.

Another report, from a very noted pathologist of one of the largest clinics in the country read "Very malignant and may be secondary to a renal or adrenal tumor." The late Dr. Jaffe had reported the tissue to be benign xanthoma and had stated that although there were numerous mitotic figures they were all regular and there was no tendency toward any malignant changes. He advised against the use of radium or x-ray as a therapy in this case.

Dr. James Ewing stated, "The tumor of the skin in a newborn infant we think is an embryonal liposarcoma. We seem to have one other case of congenital liposarcoma, but I do not remember the outcome. Your tumor looks to me quite malignant and you seem to have recurrences, which I think should be treated with radiation because this tumor ought to be radiosensitive." And he further stated "the

\* More than two years since the tumor was excised and the radium was used, there is no recurrence. The nodules have completely disappeared and the skin appears normal except for the scar.

section of tumor has the structure of a diffusely growing, fully malignant, large round and polyhedral cell liposarcoma. The cells grow diffusely, infiltrating fat tissue, and they are generally finely granular and contain many fine fat droplets. The nuclei are large and quite hyperchromatic. I should say that the grade of malignancy is very high, at least 3."

Dr. Stanley P. Reiman gave us the following report on a piece of the tumor tissue submitted to him: "It is a malignant tumor, most of the cells of which are indifferent in appearance and hence probably undifferentiated physiologically. There is fat in the section. In trying to decide whether this fat was merely invaded or a product of the tumor cells, I reached the conclusion that the latter is the case. My diagnosis is therefore liposarcoma."

This variance of opinions brings out the point that because the cells of an embryonal tumor are quite undifferentiated and usually rapidly growing it is often very difficult to state with certainty, by merely examining a tissue slide, whether the growth is malignant or benign. However, the fact that a recurrence of the tumor occurred would favor the majority of the reports that this tumor was malignant. The tumor did respond favorably to radium, although some of the pathologists considered that it would not. It is not possible always to prognosticate merely from a tissue slide the radiosensitivity of a given growth.

#### SUMMARY

1. Congenital malignant tumor of the skin in the newborn is very rare.

2. A case of congenital malignant tumor of the skin in the newborn is reported in which excision of the tumor, followed by radium therapy, gave a good result.

#### REFERENCES

1. RITTER. Angeborenes Carcinom der Haut. *Arch. f. klin. Chir.*, 5: 338-341, 1864.
2. KORTE. *Beitr. z. klin. Chir. und Beitr. z. Geburtsb. u. Gynäk.*, 90, 1870.
3. BEDFORD, G. V. A case of carcinoma of the thymus with extensive metastases in a new-born child. *Canad. M. A. J.*, 23: 197-202, 1930.
4. ANZILOTTI, A. Lesione cancerosa del labbro, trattata con la roentgenterapia in una bambina di due mesi. *Quaderni radiol.*, 4: 22-27, 1933.
5. PEARL, R., and BACON, A. L. Biometrical in pathology v. The racial and age incidence of cancer and other malignant tumors. *Arch. Path. & Lab. Med.*, 3: 963, 1927.
6. TERI, M. Adatok a csecsemokori veleszületett, rosezindulatu daganatokhoz. *Budapesti orrosi ujsag.*, 33: 857, 1935.
7. DUDITS, A., and SZABO, B. Kongenitales Melanokarzinom des Oberkiefers. *Monatschr. f. Kinderh.*, 63: 294, 1935-1936.
8. LAIN, E. S. Congenital cancer, case report. *M. J. & Rec.*, 127: 377, 1928.
9. COLLORIDI, F. Contributo alla conoscenza de tumori congeniti del lolo nel neonato. *Ann di ost. e ginec.*, 55: 387-424 (March 31) 1933.
10. CANAVAN, M. M., and HEMSATH, F. A. Glioma in the fourth ventricle of a prematurely born infant. *Arch Neurol. & Psychiat.*, 26: 1234, 1931.
11. FRANK, W. L., ENFIELD, C. D., and MILLER, A. J. Carcinoma of the tongue in a newborn child; report of a case. *Am. J. Cancer*, vol. 26, 1936.
12. PHILIPP, P. W. On carcinomas in childhood. *Ztschr. f. Krebsforsch.*, 5: 326, 1907.
13. ROSNER, S. La edad en las neoplasias cutaneas. Comentario a una estadistica personal. *Rev. A. Med. Argentina*, 49: 518, 1935.
14. DUZAN. Du cancer chez les enfants. Thèse de Paris, 1876.
15. PICOT. Les tumeurs malignes des enfants. *Rev. méd. de la suisse romanche*, 1883.
16. DEAN, A. L., JR., and PACK, G. T. Embryonal adenosarcoma of the kidney. *J. A. M. A.*, 98: 10, 1932.
17. PACK, G. T., and LEFEVRE, R. G. The age and sex distribution and incidence of neoplastic diseases at the Memorial Hospital, New York City. *J. Cancer Research*, 14.
18. RANKIN, F. W., and BRODERS, A. C. Factors influencing prognosis in carcinoma of the rectum. *Surg., Gynec., & Obst.*, 46: 660, 1928.





# INTRAPERITONEAL HEMORRHAGE IN ESSENTIAL HYPERTENSION\*

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**I**NTRAPERITONEAL hemorrhage due to the spontaneous rupture of a splanchnic vessel is rare. Ducuing and

ture was 90°F., pulse 120 and respirations 28 per minute. The thorax was symmetrical and moist râles were heard over the base of both lungs. The heart sounds were indistinct and no murmurs were heard. By percussion the heart was found to be moderately enlarged. The abdomen was distended and the presence of fluid noted. The blood Wassermann reaction was strongly positive on two occasions.

Routine treatment for congestive heart failure gave some relief. However, on January 9 the patient suddenly became very dyspneic, her skin was cold and moist and her blood pressure fell to 98/60. She failed to respond to stimulants, became comatose and expired six hours later.

*Necropsy.* The body was that of a well developed and nourished colored female, measuring 168 cm. and weighing approximately 130 pounds. The peritoneal cavity contained 800 c.c. of liquid and clotted blood. The omentum was markedly hemorrhagic and thickened and it hung freely from the transverse colon. The entire transverse colon was distended and of a dark reddish color. A partially organized blood clot was found in the midportion of the transverse colon at its junction with the mesentery. Further inspection of this area revealed a rupture of a branch of the middle colic artery at its entrance into the colon. This was responsible for the hemorrhage in the peritoneal cavity, mesentery, omentum and wall of the transverse colon. The lumen of the colon contained no free blood. The mucosa was intact throughout and there was no evidence of ulceration. The wall of the transverse colon was a dark red color due to the extravasation of blood into it and measured from 2 to 3 cm. in thickness.

The pericardial sac was moderately enlarged and the heart weighed 400 Gm. The epicardium was smooth and glistening. Cut surfaces of the heart showed marked hypertrophy of the myocardium of the left ventricle. The right auricle and ventricle were essentially negative, the endocardium smooth and intact, the valve edges free. The coronary arteries were

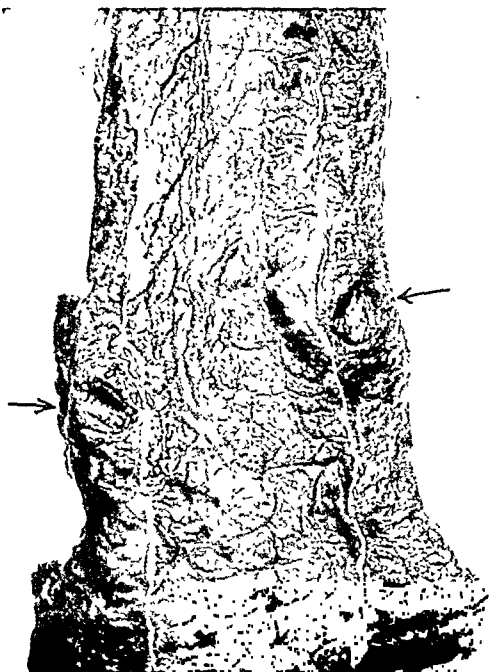


FIG. 1. Ruptured artery with hemorrhage into wall of a segment of transverse colon in a 28 year old colored female.

Florence<sup>1</sup> first described this vascular accident in 1913. In a review of the literature we collected nine additional cases.<sup>2,3,4,5,6,7,8,9</sup> The case herein presented is the eleventh. It is the only case noted in the course of 9,560 necropsies performed during the past ten years at the State Charity Hospital of Louisiana at New Orleans.

## CASE REPORT

The patient, a colored female, aged 28 years, was admitted on January 6, 1937 with complaints of shortness of breath, cough and weakness. For the previous month these symptoms had progressed.

She was markedly dyspneic and cyanotic, with a blood pressure of 260/180. Her tempera-

\* From the Departments of Pathology and Bacteriology, State Charity Hospital of Louisiana and the School of Medicine, Louisiana State University, New Orleans.

patent throughout. The thoracic aorta showed longitudinal wrinkling throughout the ascending and descending portions.

The right kidney weighed 130 Gm., the left 135. The capsule was stripped with slight difficulty, revealing a dark red finely granular surface with a few scattered petechial hemorrhages. The cut surfaces of the kidneys showed the cortex to be slightly narrowed.

## DISCUSSION

The association of rupture of a splanchnic artery with hypertension is rather definite, since in seven of the eleven cases reported there was high blood pressure. In the six cases in which the condition of the artery was mentioned all showed marked arteriosclerosis. In the second case of Moorehead

CHART I  
REPORTED CASES OF RUPTURE OF SPLANCHNIC VESSELS

No.	Author	Year	Age Sex	Complaint	Site	Blood Pressure	Arteriosclerosis of Ruptured Vessel	Operation	Result	Autopsy
1	Ducuing and Florence	1913	Young woman	Abdominal pain, 8 months pregnant, in labor.	Branch of superior mesenteric artery.	?	?	.....	Died	Yes
2	Starcke	1923	M—60	Severe epigastric pain.	Gastroduodenal artery.	155 systolic two years.	Marked	Ligation	Recovered	
3	Budde	1925	M—27	Severe abdominal pain.	Left gastroepiploic artery.	?	?	Ligation	Recovered	
4	Green and Powers	1931	F—54	Severe abdominal pain.	Left gastric artery.	6 months before operation 270 systolic, 8 months after operation 260/145	Marked	Ligation	Recovered	
5	Mourque-Molines, Cabenac	1933	M—56	Vomiting, gastric upset.	Left gastric artery.	Severe.	Marked	Ligation	Recovered	
6	Thompson, Dunphy	1935	F—62	Precordial pain shock.	Branch of left gastric artery.	Marked hypertension for 6 years. Blood pressure 170/100 two weeks before admission.	Marked	?	Recovered	
7	Buchbinder and Green	1935	M—57	Severe abdominal pain.	Right gastric artery.	Ten days after operation 190/115.	Marked	Ligation	Recovered	
8	Moorehead and McLester	1936	M—44	.....	Junction of right and left gastric arteries.	High blood pressure for several years.	.....	.....	Died	Yes
9	Moorehead and McLester	1936	M—50	Dyspnea.	Superior mesenteric artery.	220/140. Patient treated in ward for hypertension. 280/160.	Marked	.....	Died	Yes
10	Lafferty and Pearson	1938	F—28	Shock, dyspnea.	Superior mesenteric artery	.....	.....	.....	Died	Yes
11	Morton	1938	M—72	.....	Branch of superior mesenteric artery.	.....	.....	Not ligated	Recovered	

Histologic examination of the lungs, heart, muscles, pancreas, spleen and liver showed nothing of note. The kidneys revealed thickening and hyalinization of the afferent arterioles, with occasional hyalinization of the glomerular tufts. The picture was consistent with renal arteriosclerosis of moderate degree. The aorta showed perivascular round cell infiltration and endarteritis in the vasa vasorum. The middle colic artery showed no apparent pathology. Sections taken through the transverse colon showed marked hemorrhage into the entire wall.

and McLester in addition to the arteriosclerosis and rupture, the various coats of the superior mesenteric artery were separated for a distance of several centimeters by a dissecting hemorrhage. In a series of hypertensive cases Bell<sup>10</sup> found 15 per cent with cerebral hemorrhage. In a series of 497 cases of hypertension from the post-mortem records of the Charity Hospital of the State of Louisiana at New Orleans, Decherd and Schenken<sup>11</sup> found that 17.7 per cent had cerebral hemorrhage.

It is possible that the rarity of this vascular accident is associated with the infrequency of arteriosclerotic changes in the vessels of the gastrointestinal tract. Thus Brooks,<sup>12</sup> in a study of 368 cases of arteriosclerosis, found in only nine macroscopic evidence which involved the celiac axis and its branches. Only four cases of arteriosclerosis involving the mesenteric arteries were encountered in his series. Kummel,<sup>13</sup> in a study of the superior mesenteric artery in thirty-nine individuals over 40 years of age, found medial calcification in only one.

In five of the cases reported the rupture occurred in the right or left gastric artery. In addition to the hemoperitoneum, a characteristic hematoma was present in the gastrohepatic omentum. In Starcke's case the rupture occurred in the gastroduodenal artery and in the case of Budde the left gastroepiploic artery. Thus in seven of the ten cases the rupture occurred in arteries emanating from the celiac plexus. In only four cases was the superior mesenteric artery involved (Ducuing and Florence; Moorehead and McLester's second case; Morton; and the case herein presented). In the first case reported in the literature there was no record of the blood pressure or condition of the artery.

Six of the cases occurred in males and four in females. The youngest patient was that of Budde 27 years of age, the oldest that of Morton, 72. The peak of the incidence is in the fifth decade.

In the majority of the cases the chief clinical symptoms were acute abdominal pain in the region of the epigastrium, associated with rigidity of the abdominal muscles and varying degrees of shock. Seven of the patients were operated on and all recovered. The remaining four patients were examined after death.

#### SUMMARY

Our case represents the eleventh example of intra-abdominal hemorrhage due to the rupture of a splanchnic artery. Most of the cases occur in the right or the left gastric artery. One occurred in the gastro-

duodenal and one in the left gastroepiploic artery. Only four cases of the superior mesenteric artery have been noted, including the present case. The association with severe hypertension is rather striking as it occurred in seven of the eleven cases. Six cases showed definite marked arteriosclerosis of the rupture vessel. We feel that hypertension, severe gastrointestinal vascular sclerosis, separately or in combination, are decided factors in the precipitation of rupture of the vessel, comparable to cerebral hemorrhage in hypertension. The infrequency of this accident is probably in part due to the infrequent findings of vascular sclerosis in the intestinal arteries. The clinical symptoms are severe abdominal pain associated with varying degrees of shock. All the patients operated on recovered completely.

#### REFERENCES

1. DUCUING, M., and FLORENCE, M. Contusion du rein. Hémopéritoine. Guérison spontanée. Valeur diagnostique de la ponction exploratrice du cul-de-sac de Douglas. *Bull. et mém. Soc. de chir. de Paris*, 39: 645, 1913.
2. STARCKE, G. Spontaneous rupture of gastroduodenal artery. *Ugeskr. f. Laeger.*, 85: 963-964 (Dec. 27) 1912.
3. BUDDE, M. Spontaneous rupture of gastroepiploic artery. *München. med. Wchnschr.*, 72: 1383-1384 (Aug. 14) 1925.
4. GREEN, W. T., and POWERS, J. H. Intra-abdominal apoplexy. *Ann. Surg.*, 93: 1070-1074, 1931.
5. MORQUE-MOLINES, E., and CABENAC, E. Abondante hémorragie intra-péritonéale par infarctus de l'épiploon-gastro-hépatique. *Bull. et mém. Soc. nat. de chir.*, 59: 720-727 (May) 1933.
6. THOMPSON, K. W., and DUNPHY, J. E. Intra-abdominal apoplexy. *Ann. Surg.*, 102: 1116-1118 (Dec.) 1935.
7. BUCHBINDER, J. R., and GREEN, E. T. Intra-abdominal apoplexy. *J. A. M. A.*, 105: 874-875 (Sept. 14) 1935.
8. MOOREHEAD, M. T., and MCLESTER, J. S. Abdominal apoplexy. *J. A. M. A.*, 106: 373-374 (Feb. 1) 1936.
9. MORTON, C. B. *Arch. Surg.*, 36: 723-728 (May) 1938.
10. BELL, E. T. *Textbook of Pathology*. Philadelphia, 1938. Lea and Febiger.
11. DECHERD, G. JR., and SCHENKEN, J. R. Unpublished data.
12. BROOKS, H. A preliminary study of visceral arteriosclerosis. *Am. J. M. Soc.*, 131: 778, 1906.
13. KUMMEL, R. Ueber die sklerose der Eingeweidearterien der Bauchhöhle. *Zentralbl. f. allg. Path. u. path. Anat.*, 17: 1929, 1906.

# OSTEOCHONDRITIS DISSECANS\*

## REPORT OF CASES INVOLVING ELBOW, ANKLE AND METATARSOPHALANGEAL JOINTS

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**O**STEOCHONDRITIS dissecans involving a joint other than the knee is relatively rare; of the reported cases, those involving the knee joint comprise over 85 per cent.<sup>1</sup> The elbow joint is next in order of frequency but only occasional cases have been reported involving the hip, ankle or metacarpophalangeal joints. In this communication we report a case of the lesion occurring in each of the following: capitellum of the humerus, talus, and head of a metatarsal.

Wagoner and Cohn<sup>2</sup> have defined osteochondritis dissecans as "a noninfectious process involving the articular cartilage and the subchondral bone of certain long bones of the extremities, which, by, sequestration from the articular surface, usually produces a single foreign body, or, more rarely, two, in the contiguous joint. This body is originally of an osteocartilaginous composition, but its structure subsequently undergoes alteration by the fluid of the joints." The cause of the lesion is unknown. The relationship of the etiology to trauma has evoked considerable discussion and numerous theories of causation have been evolved. The balance of evidence is in favor of a traumatic causation but the mechanism of the detachment of the loose fragment has not been demonstrated. It is noted that trauma had an important part in the development of this lesion in the following cases.

**CASE 1.** H. G. B., a white soldier of 28 years, was admitted to the hospital on December 20, 1937 with complaints of pain and tenderness over the lateral aspect of the right

elbow and inability completely to extend the joint. He was a baseball pitcher of his organization team and for twenty-three months prior to hospitalization had recurrent attacks of pain and stiffness of the right elbow. On September 26, 1937, while throwing a baseball, he heard a snap in the elbow followed by considerable pain and tenderness over the lateral aspect of the joint and inability to extend the forearm.

*Examination.* He was a well developed and well proportioned adult male without evidence of endocrine disturbance. There was moderate tenderness over the entire extensor and lateral aspects of the right elbow. Extension of the joint was limited to 135 degrees. Roentgenographic examination revealed a loose body in the right elbow joint and a defect in the capitellum of the humerus. The blood Wassermann test was negative.

*Treatment.* An arthrotomy was done December 22, 1937 at which time a body lying entirely loose in the joint was removed (Fig. 1), and the cavity in the capitellum of the humerus from which the body was derived was curetted. The operative wound healed by primary intention. On January 6, 1938 physiotherapy was started with whirlpool, massage and active exercise. Recovery was rapid with prompt return of full range of motion and excellent function of the joint. On January 23, 1938 he was discharged from the hospital and returned to full military duty. He has remained free from symptoms referable to the elbow since discharge from the hospital.

*Comment.* Miller<sup>3</sup> reported a case of osteochondritis dissecans of the capitellum of the right humerus occurring in a newsboy. He attributed the lesion to the trauma incident to the throwing of newspapers while the boy was working on his news-

\* From the Surgical Service, Tripler General Hospital. Published with the permission of the Surgeon General, U. S. Army.

paper route. The mechanism of the production of the lesions in these two cases was the same and they increase the evidence that

swollen and there was marked tenderness over the medial aspect of the joint. Flexion of the foot on the leg caused severe pain in the ankle.

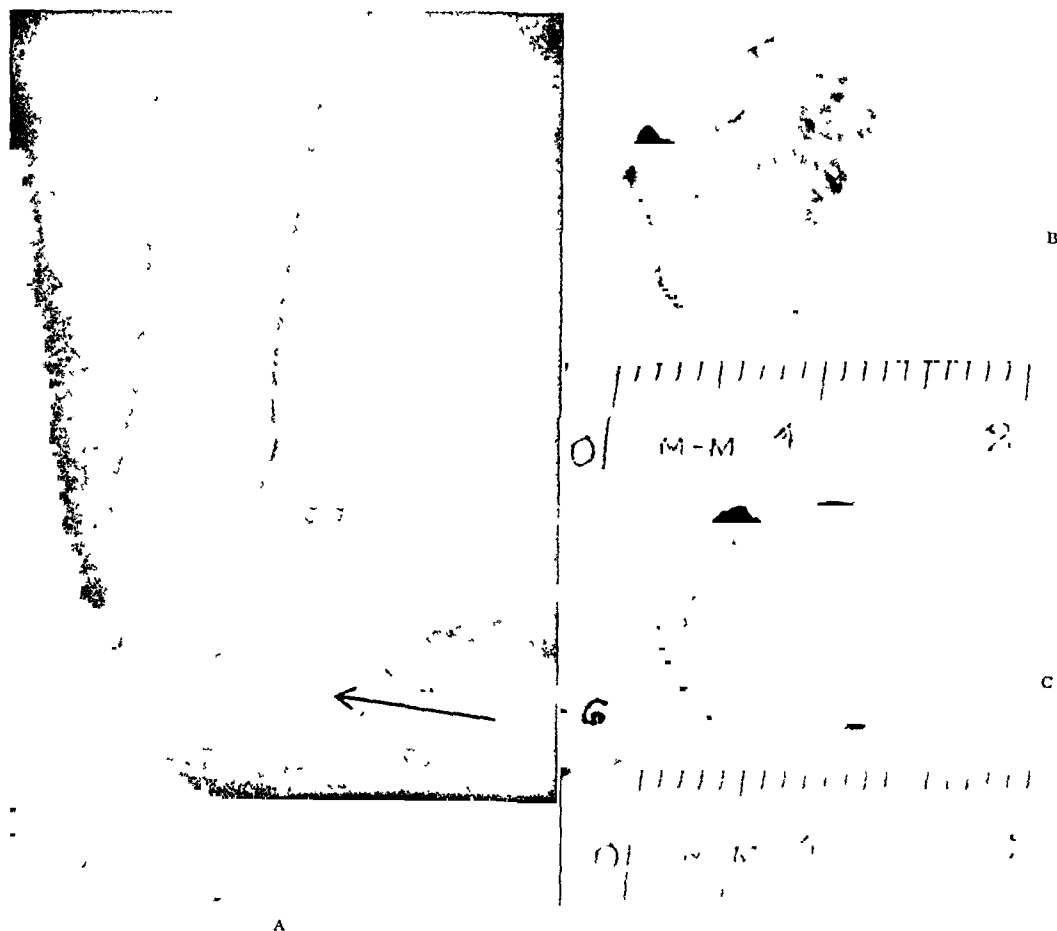


FIG. 1. Case I. A, roentgenogram showing body lying free in elbow joint. B and C, views of loose body following its removal from the joint.

osteochondritis dissecans may be caused by slight repeated trauma.

**CASE II.** M. W. H., a white soldier of 22 years, was admitted to the hospital on August 9, 1937 with complaints of pain in the right ankle on weight bearing, which was most marked on flexing the joint. On July 2, 1937 this man was struck on the medial aspect of his right ankle by a rolling 50 gallon drum of oil which sharply inverted his foot. This injury was followed by the symptoms given above which persisted without significant change in severity to the time of admission.

**Examination.** This man was well developed and well proportioned. There was no evidence of endocrine disturbance. The patient was unable to bear weight on right foot because of pain in the ankle. The ankle was moderately

Roentgenographic examination (Fig. 2) revealed a partially detached body and an excavation on the superior surface of the talus. The blood Wassermann test was negative.

**Treatment.** The right ankle was immobilized by a plaster cast on August 10, 1937. The cast was removed on September 13, 1937. Roentgenographic examination at this time showed no change in the lesion. Physical findings were essentially the same as on admission except for the disappearance of the swelling about the joint. An arthrotomy was done on September 24, 1937. A partially separated body approximately 1.5 cm. in diameter was found. This was held in place by a broad area of intact articular cartilage. This attachment was incised and the excavated area of the talus curetted. Physiotherapy and partial weight bearing were started October 20, 1937. The patient made a satis-

factory recovery and function of right ankle was excellent with the exception of slight tenderness on marked flexion which persisted for several months following discharge from the hospital. On December 5, 1937 he was discharged from the hospital and returned to full military duty part of which consisted of infantry drill. This he was able to perform without difficulty.

*Comment.* This case was seen early in the course of development of the lesion and prior to the detachment of the body from its bed. Immobilization for the joint by a plaster cast was entirely without benefit in a case in which the body was only partially separated; if at all indicated, this is the type of case in which this type of treatment would be expected to show beneficial results. This experience gives further evidence that the treatment of osteochondritis dissecans is surgical irrespective of the stage of development of the lesion.

CASE III. G. W., a white soldier of 56 years, was admitted to the hospital on February 24, 1938 complaining of painful corns on the third toe, left foot. In 1918 this man dropped a projectile on his left foot. Following this injury the third toe of this foot developed the shape of a hammer toe. Except for a short period immediately following the injury there had been no pain on movement of the toe and no difficulty in walking. However, because of the shape of the toe, the rubbing of a shoe caused painful corns to form on the dorsum of the toe and on the neighboring toes. He came to the hospital requesting relief during a period when his corns were particularly painful.

*Examination.* He was a well developed, obese, adult white male. Obesity was present, but was not believed to be due to endocrine disturbance. He had a persistent arterial hypertension of approximately 230 systolic and 130 diastolic measured in millimeters of mercury. Retinal examination revealed an arteriolar sclerosis. Physical, roentgenographic and electrocardiographic examination of the heart revealed findings compatible with a diagnosis of hypertensive heart disease of an essential type. Blood chemistry and urine examinations were within normal limits. All toes of both feet were normal

in appearance with the exception of the third toe, left foot, which was a hammer toe. On the dorsal, lateral and medial aspects of the proxi-



FIG. 2. Case II. Roentgenogram of right ankle showing osteochondritis dissecans involving the superior articular surface of the right talus.

mal interphalangeal joint of this toe were large tender corns. The blood Wassermann test was negative.

*Treatment.* The third toe, left, was disarticulated at the metatarsophalangeal joint on February 25, 1938. The articular surface of the base of the proximal phalanx was found to be quite misshapen, the articular cartilage of the head of the metatarsal and a calcified loose body were lying loose within the joint. (Fig. 3.) A roentgenogram taken following the operation shows the condition of the head of the metatarsal. (Fig. 3.) There was delayed healing of the operative wound due to a low grade infection of the proximal angle of the wound, but it was well healed by March 15, 1938. On April 4, 1938, he was returned to full military duty which he has performed without difficulty since that time.

*Comment.* This case is instructive in that there was a traumatic derangement of a metatarsophalangeal joint severe enough

2. The lesion may be produced by traumata varying widely in type and intensity from a single, severe crushing

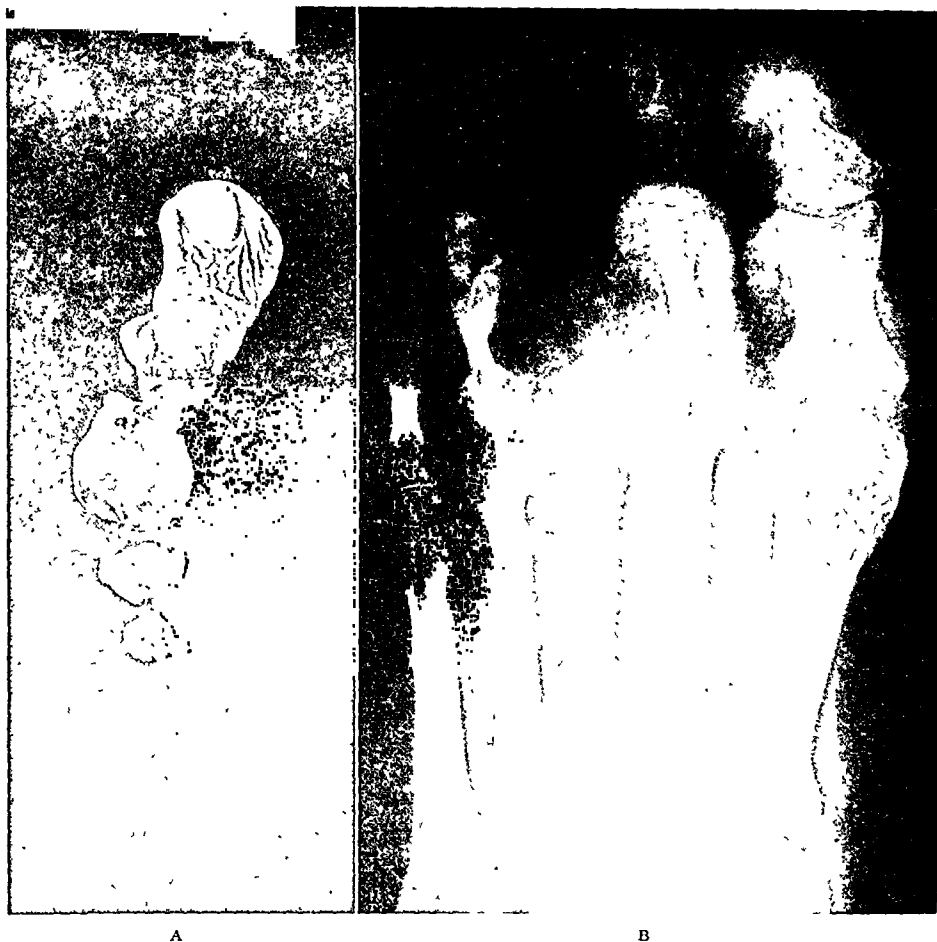


FIG. 3. Case III. A, third toe of left foot following disarticulation at the metatarsophalangeal joint and two loose bodies which were found within the joint space. B, roentgenogram of foot taken following removal of the toe. Note deformity of head of third metatarsal resulting from osteochondritis dissecans of twenty years' duration.

to produce a hammer toe of twenty years' duration. This resulted in no disability other than that incident to painful corns the result of pressure of a shoe on the deformed toe although this man's duties required extensive use of his feet.

#### SUMMARY

1. Three cases of osteochondritis dissecans are reported occurring in joints other than the knee, i.e., elbow, ankle, and metatarsophalangeal joints.

injury to a mild, repeated injury resulting from the forces brought into play by joint movements.

3. The treatment is the surgical removal of the detached fragment.

#### REFERENCES

1. CONWAY, F. M. Osteochondritis dissecans. *Am. J. Surg.*, 38: 691, 1937.
2. WAGONER, G., and COHN, B. N. Osteochondritis dissecans. *Arch. Surg.*, 23: 1, 1931.
3. MILLER, L. F. Osteochondritis of the capitellum of humerus. *Radiology*, 27: 237, 1936.

# PRIMARY CARCINOMA OF THE FALLOPIAN TUBES\*

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PRIMARY tumors of the fallopian tubes are among the rarest of new growths. This is difficult of explanation in view of the great frequency of such growths in the other female pelvic organs.

Tubal tumors are well classified by Watkins<sup>1</sup> into those arising from epithelial cells, connective tissue, or from embryonal cell rests. The primary tumors originating from epithelial tissue include carcinoma, endometrioma, adenoma, papilloma, endothelioma, cysts, and chorionepithelioma; from connective tissue, fibroma, lymphangioma, lipoma, and sarcoma; from embryonic cells, dermoids and teratoma. Among these tumors carcinomata are the most common.

Some idea of the rarity of fallopian cell carcinoma is shown by the fact that Vest<sup>2</sup> found only four cases in 19,000 gynecological admissions to the Hopkins Hospital, and Barrows,<sup>3</sup> three cases in 30,000 such admissions at Bellevue Hospital. Holland<sup>4</sup> reported nine cases in 10,000 complete salpingectomies from the Mayo Clinic. At the University Hospitals, Cleveland, we find but two cases in 22,300 strictly gynecological admissions, not including 62,000 general surgical admissions, at least one-sixth of which were for pelvic diseases in women; in all, a general average of about one case in 10,000 gynecological admissions, or one primary carcinoma in every 1,000 salpingectomies.

The condition was first described macroscopically by Renaud<sup>5</sup> in 1847. Orthman,<sup>6</sup> in 1886, gave the first accurate description and pathology of the condition. In 1910 Doran<sup>7</sup> tabulated 100 cases, and in 1925 Bower and Clark,<sup>8</sup> in an excellent paper, reviewed 133 cases. In 1929 Wharton and Krock<sup>9</sup> brought the subject up to date

with a collection of 244 cases. Since then, occasional reports of one or two cases, by McGlinn and Harter<sup>10</sup> and others, have brought the total to probably not more than 275 cases at the present time. The condition, though rare, is no doubt often and easily overlooked, being mistaken for an ordinary pelvic inflammatory state. This is yet another reason to urge a most careful gross examination at operation and a complete microscopic examination of all tissues removed surgically. If carcinoma is recognized at operation, a complete hysterectomy is imperative; if not until later, postoperative deep x-ray or radium may do much to improve the present poor results.

The etiology is unknown. Many authors have suggested the important influence of a pelvic inflammatory condition, but many afflicted women have never had such a condition. Considering the great frequency of pelvic inflammation, we would expect to see many more cases of tubal carcinoma if the inflammation were a pertinent factor. Tuberculosis of the tube seems to be more frequently coincident than one would expect and may be of importance in stimulating the formation of benign papillomata which subsequently become malignant. Here we must urge greater accuracy in the pathologic diagnosis as we have seen several reproduced photomicrographs of tuberculous salpingitis which have been reported as primary carcinoma. The hypertrophied epithelium and epithelial cells, which due to the manner of section are often seen out in the muscular or connective tissue layers, have been mistaken for malignant cells.

We now not infrequently recognize endometrial implants in the tube, and it

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may be possible, as Kelly<sup>11</sup> suggests, that certain tubal carcinomas, especially the adenomatous and medullary types, have their origin in this aberrant tissue.

Primary tubal carcinoma is about equally frequent in parous and non-parous women, so that fertility is not influential. Age does not seem to be significant, and although this carcinoma is most common in the fifth decade, Bower and Clark's patient was 25, Holland reported a case in a woman of 26, Norris<sup>12</sup> in one of 29, Novy<sup>13</sup> 70, and Jacob<sup>14</sup> in one of 73 years. One of the cases we have to report was in a woman 80 years old, the oldest case on record so far as we can learn.

About one-third of all cases are bilateral when recognized. This may be due to independent development or to direct extension through the uterine cavity, transperitoneal migration, or from metastases from the other tube by way of the blood or lymphatic channels. The tube is frequently involved secondarily to carcinoma of the ovary or fundus, as well as occasionally from carcinoma of the cervix, stomach, or gall-bladder. Secondary involvement is ten times as common as a primary growth. If the growth is primary, it usually starts in the tubal mucosa; if secondary, in the wall of the tube or on its peritoneal surface.

The most common primary carcinoma of the tube is papillary in type, the advanced stage of which may be adenomatous in appearance. Both pictures are frequently seen in the same growth. These papillary carcinomas may develop from benign papillomata or arise independently from the tubal mucosa. They occur usually in the outer half of the tube, the fimbriated end of which closes early, though the uterine end does not, and the tumor may be felt as a soft, loose mass through the distended, clubbed, thin-walled, sometimes fluctuant tube. The medullary carcinomas are usually firmer and fibrous, though like the papillary growths they may be cystic. Peritoneal adhesions are not common in early cases and the tube

looks like a hydrosalpinx, but is firmer, sausage-shaped, and contains a purulent, sanguinous fluid or grumous mass. The tumors are from 1 to 1.5 cm. in diameter, depending somewhat upon the duration.

Gross differentiation from benign papillomata is often very difficult. With the benign tumors the fimbriated end of the tube is more often open and the cauliflower-like growth, which is not ulcerated or necrotic, may protrude. Benign growths show no local or distal signs of invasion.

Microscopically the benign tumors show usually but a single layer of epithelial cells covering the villi or lining the gland-like spaces formed by adherence or coalescence of the villi. The epithelial cells are uniform in size and shape, as are their nuclei, and all stain uniformly. Nuclear figures and cellular division are rare and there is no evidence of cellular penetration or invasion of the underlying structures.

If the growth is malignant, the epithelial cells are in most cases several layers deep, irregular in size and shape, with irregularly staining large nuclei. A marked vacuolization of the cells and nuclei is often seen. Mitoses are common. Invasion of the tube wall is relatively late or may be absent. The sub-epithelial connective tissue shows round cell infiltration. The tubal epithelium is normal except where involved. When adenomatous in appearance, the picture is not unlike adenocarcinoma of the fundus. Endometrioma, tuberculosis, and chronic inflammation of the tubal wall are to be carefully differentiated, especially from the medullary type of carcinoma.

The peritoneum, ovary or fundus may be involved through metastases or by direct extension. Implantation on the endometrium is very rare. Distant metastases and glandular involvement occur early and are seen in one-third of all cases. The superior lumbar, inguinal, external iliac, hypogastric and sacral lymphatics being most often affected.

Meigs<sup>15</sup> states that in 396 cases of carcinoma of the cervix, there were metastases to the tube in six, 1.5 per cent;

in 122 carcinomas of the fundus, three, or 2.5 per cent showed the tube involved; and in 131 carcinomas of the ovary, the tube showed metastases in six, or 4.5 per cent. He emphasized the difficulty, due to the similarity in microscopic appearance, in differentiating between primary and secondary growth in the tube when the fundus or ovary is also involved. The growth may simulate a squamous carcinoma and be the result of metaplasia of the tubal epithelium or a direct extension from the cervix.

There are no distinctive symptoms. More often than not there is some slight disturbance of menstrual function with some increase in frequency and irregularity. Post-menopausal bleeding may occur. A free, clear, or slightly bloody watery discharge, which occurs constantly or intermittently, and often comes in gushes, is suggestive. A foul odor indicates necrosis. Pain referred to the lower abdomen is earlier than with carcinoma of the cervix or fundus, and is probably due to stretching and muscular activity of the tubal wall, as with an ectopic pregnancy.

With any of the above symptoms, the finding of a normal cervix, fundus and ovaries, and the presence of a soft, unilateral mass, should make one suspicious, especially if there be some blood-stained free fluid in the abdomen. Very rarely may minute fragments of cancer tissue be found in the watery discharge from the vagina. This should be collected, filtered, and any sediment examined microscopically. If, as in one of our cases, diagnostic curettage shows very little tissue, but the presence of carcinoma, especially of a papillary type, the correct diagnosis is probable.

If the diagnosis can be made in advance, or is made at operation, the treatment is pan-hysterectomy with removal of both tubes and ovaries. Postoperative deep x-ray or radium therapy is always indicated.

Unfortunately the symptoms are not striking. The disease progresses rapidly and most cases are advanced, adherent, and with glandular involvement when first

seen. The prognosis is poor, recurrences are common and early, and but few five-year cures are obtained. Bower and Clark<sup>8</sup> reported the mortality in 133 collected cases. In eighty cases in which the operation was incomplete, 56 per cent died. Other organs were involved in forty-three of the forty-five deaths. In fifty-three cases of which twenty-one had local metastases, but in which complete operation was done, the mortality was only 34 per cent. These figures are excellent but misleading as many cures were reported of patients still convalescent. They do show, however, the superiority of the complete operation. Lipschitz<sup>16</sup> reported only four four-year cures in 122 cases, and Graves<sup>17</sup> estimated the five-year cures at not over 4 per cent.

#### REPORT OF CASES

CASE 1. R. G., was admitted to University Hospital, July 7, 1934. She was then 80 years old and had had two children. She complained of slight spotting for the previous four months, at first infrequent, more recently almost constant. There was at times some brownish, malodorous, watery discharge. Occasionally she had some slight cramp-like discomfort in the lower abdomen. For two years she had had a chronic pyelitis and low grade chronic cystitis with occasional dysuria. Menopause had occurred thirty-four years before. A malignant right breast had been removed twenty years previously.

The patient was mentally alert. Physical examination was essentially negative. The urine showed a trace of albumin and a few hyalin casts. Pelvic examination showed a contracted senile vagina and normal cervix. The fundus was small, forward and movable. The right ovary was very small and movable. On the left there was a movable, semi-fluctuant, elongated mass, giving the impression of a hydro- or hematosalpinx.

A diagnostic curettage was done under nitrous oxide anesthesia. The cervical canal was located with much difficulty and was very stenosed and tortuous. When the probe was withdrawn, perhaps 1 ounce of straw-colored fluid escaped, which on examination was found not to be urine. This fluid was filtered and a few recovered shreds of tissue included with the very sparse uterine scrap-

ings. Very fortunately these showed microscopically the presence of a papillary carcinoma. (Fig. 1.)

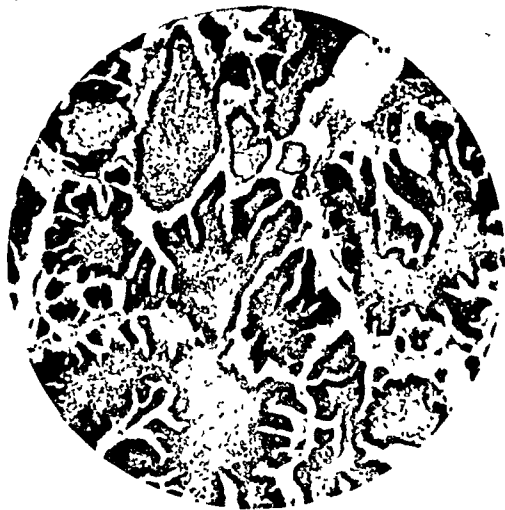


FIG. 1. Papillary adenocarcinomatous tissue from tube, removed from uterine cavity in hydrometrial fluid by diagnostic curettage.

malignant growth of the uterine body. The optional treatment with radium or hysterectomy was given the patient. Considering her age, we advocated radium, but the patient insisted upon operation.

Three days after curettage, laparotomy was done under spinal anesthesia (spinocaine 3 c.c.). The uterus was slightly enlarged, the right tube and ovary normal, but both very atrophic. The left tube was smooth and glistening, grayish pink in color, and was distended to about 2 cm. in diameter, approximately 15 cm. long, sausage-shaped, the fimbriated end closed, the wall almost transparent. A soft, movable mass and fluid were palpated in the lumen. The only pelvic adhesion was one very light one from the left tube to the sigmoid. A pan-hysterectomy with bilateral salpingo-oophorectomy was quickly and easily done.

The patient made a very satisfactory recovery and was discharged on the sixteenth day and remained perfectly well for eight months when she rapidly developed an ascites and



FIG. 2. Gross specimen. Case 1. All structures normal except left tube which is distended by papillary carcinoma within the lumen. Fimbriated and closed.

It was hard to correlate the presence of such a growth in the fundus with the very scanty scrapings, and in the light of our present knowledge would have led to a correct preoperative diagnosis. At the time we felt we were dealing with an unusual type of

nodules deep in the abdominal wall, both of which are undoubtedly due to metastases and indicate an early exitus.

The very careful pathologic examination with serial sections was negative for all tissue except the left tube. This had an average

diameter of 18 mm. and was somewhat club-shaped. Weight of the entire specimen was 30 Gm. (Fig. 2.) Sections through the wall

to many cell layers thick and in places formed a solid mass of cells with a marked adenomatous appearance. (Fig. 4.) The individual cells and



FIG. 3. Large papilla with small base from tube wall at A. Note large amount of connective tissue and variation in thickness of epithelial covering.



FIG. 4. Marked adenomatous appearance occasioned by coalescence of papillae. Note sparsity of connective tissue and vacuolization of epithelial cells.



FIG. 5. Gland-like spaces lined by epithelial cells which are irregular in size and shape. Cells and nuclei vary in staining density. Mitoses and cell division common. Marked vacuolization in cells.

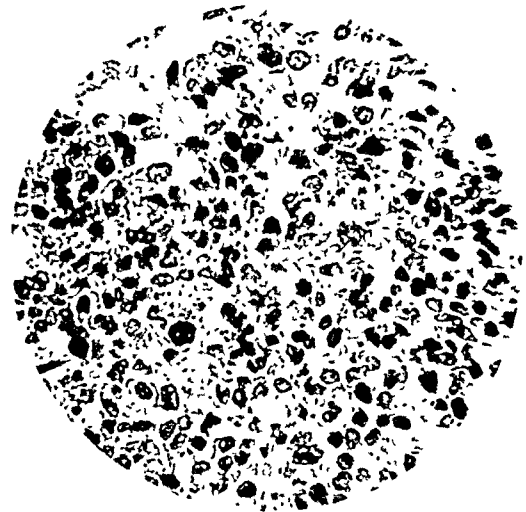


FIG. 6. Section from tube. Case 11. Malignant cells with very little stroma. Irregularity in size and shape of nuclei which are hyperchromatic. Vacuolization and nuclear figures seen.

revealed a thin, translucent tissue, probably the remains of both the serosa and muscularis, and the entire lumen was filled with a grayish pink, friable, granular tissue, which was mottled with pinpoint yellow areas. The lumen was lined by an irregular layer of columnar epithelium from which many small buds and complex papillae arose. Some papillae had a very substantial connective tissue framework (Fig. 3) others almost none. The epithelial covering was most irregular, varying from one

their nuclei varied greatly in size and shape, as well as in staining characteristics. Hyperchromatism was marked. Cell division and nuclear figures were common, and of special interest was the marked vacuolization of many of these cells. (Fig. 5.) Primary adenopapillary carcinoma of the left tube was the final diagnosis.

CASE 11. J. J., was admitted April 20, 1934. She was 52, para i, had had three miscarriages.

Menopause had occurred three years previously and no vaginal bleeding had been noted since. She complained of an abdominal enlargement noted for the past three months; radiating pains down the legs; difficulty in starting urination; and a one-year's increase in weight from 117 to 146 pounds.

Physical examination showed a distended abdomen with free fluid present. A firm, irregular mass was felt in the midline of the lower abdomen extending to the umbilicus. The cervix was normal, the uterus could not be made out separate from the mass which filled the pelvis and was fixed. The urine contained a moderate trace of albumin and a few casts. Wassermann was negative as were x-rays of the chest.

Exploratory laparotomy was done under local anesthesia. Nine quarts of straw-colored fluid were evacuated. The omentum was adherent to the parietal peritoneum and to the pelvic structures which were inseparably matted together. The aortic and mesenteric lymph glands were enlarged and the liver contained metastases. A mesenteric gland was removed for biopsy and the abdomen closed. The patient died one month later. Autopsy showed metastases to the lungs, abdominal lymphatics, liver, peritoneum, and both ovaries, neither of which was enlarged or cystic. The stomach, gall-bladder and intestines were normal. Both tubes were enlarged, thickened and closed.

Sections of the tubes showed some few areas of normal tubal mucosa, but mostly tumor tissue which filled the lumen and had deeply infiltrated the musculature. The growth was composed of large, polyhedral epithelial cells varying in size as did their nuclei, which were vesicular and irregular in staining. Many dividing cells and nuclear figures were seen. (Fig. 6.) In some areas there was a suggestion of gland formation. The tube was considered the origin of the primary tumor, but it was impossible to say whether primary in one tube or bilateral. All metastases were similar in cell structures to the tubal tumor. Primary carcinoma simplex of the fallopian tube with metastases was the ultimate diagnosis.

#### SUMMARY

1. Primary carcinoma of the fallopian tube, though rare, is undoubtedly often overlooked. It occurs about once in every 10,000 gynecological cases. Many reported

cases have apparently been incorrectly diagnosed.

2. Symptoms and signs are not specific. The cervix is normal, the fundus not usually pathologic. A soft, semi-fluctuant mass may be felt in the position of the tube. Slight irregularities in menstruation or post-menopausal spotting are common. A slight, continuous or intermittent watery discharge, which often comes in gushes, is suggestive. The finding of papillary carcinomatous tissue in this discharge, or at diagnostic curettage, yielding very little scrapings, is very suggestive evidence.

3. The disease is usually advanced when first seen. Metastases occur early and the end results are very poor, with probably not over 5 per cent five-year cures.

4. Pan-hysterectomy and the removal of both tubes and ovaries is the only treatment worthy of trial. Postoperative deep x-ray therapy or radiation should be given.

5. The condition should always be borne in mind and all tissues carefully examined grossly at operation as well as microscopically postoperatively.

#### REFERENCES

1. WATKINS, R. E. *Obstetrics and Gynecology*, Vol. 2. Philadelphia, 1933. W. B. Saunders.
2. VEST, C. W. *Bull. Johns Hopkins Hosp.*, 25: 305, 1914.
3. BARROWS, D. N. *Am. J. Obst. & Gynec.*, 13: 710, 1927.
4. HOLLAND, W. W. *Surg., Gynec. & Obst.*, 51: 683, 1930.
5. RENAUD. Quoted by Holland.<sup>4</sup>
6. ORTHMAN. *Zentralbl. f. Gynäk.*, 10: 816, 1886.
7. DORAN, A. J. *Obst. & Gynec. Brit. Emp.*, 17: 1, 1910.
8. BOWER, J. O., and CLARK, J. H. *Arch. Surg.*, 11: 586, 1925.
9. WHARTON, L. R., and KROCK, F. H. *Arch. Surg.*, 19: 848, 1929.
10. MCGLENN, J. A., and HARRER, W. B. *Am. J. Obst. & Gynec.*, 26: 354, 1933.
11. KELLY, H. A. *Gynecology*. New York, 1928. D. Appleton.
12. NORRIS, C. C. *Surg., Gynec. & Obst.*, 8: 272, 1909.
13. NOVY. *Monatschr. f. Geburtsh. u. Gynäk.*, 11: 1043, 1900.
14. JACOB. In discussion of Norris' paper.<sup>12</sup>
15. MEIGS, J. V. *Tumors of the Female Pelvic Organs*, p. 485. New York, 1934. Macmillan.
16. LIPSCHITZ, K. *Monatschr. f. Geburtsh. u. Gynäk.*, 39: 33, 1914.
17. GRAVES, W. P. *Gynecology*, p. 535. Philadelphia, 1928. W. B. Saunders.

# NEW INSTRUMENTS

## THE BUIE SIGMOIDOSCOPE

AN ALTERATION IN ITS DESIGN TO FACILITATE DIFFICULT EXAMINATIONS

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IT is often difficult or impossible to insert the sigmoidoscope, which is 10 inches (25 cm.) long and  $\frac{5}{8}$  inch (1.8 cm.) in diameter, in those patients who have lesions within the bowel which decrease the normal diameter of the rectum, recto-sigmoid or sigmoid, or who have lesions external to the bowel which alter its normal location or distort its normal contour, or in patients in whom the normal mobility of this portion of the bowel is limited. Frequently, in such patients, however, it is possible to introduce a sigmoidoscope which is 10 inches (25 cm.) long but only  $\frac{7}{16}$  inch (1.2 cm.) in diameter. In treating such patients as these, because of the presence of the abnormality, a thorough examination is imperative in spite of the fact that they are usually weaker and often less coöperative than those in whom the bowel is normal.

The sigmoidoscopic examination is usually attempted primarily with the larger Buie sigmoidoscope, which is easier to introduce through the lumen of the bowel because of the larger field which it exposes to the examiner's view. It has been necessary to withdraw the larger sigmoidoscope and then introduce the smaller one through the same portion of the bowel, a time-consuming and often uncomfortable manipulation.

Recently, with the assistance of Mr. Thorvald Maijgren, two types of Buie sigmoidoscopes have been altered to facilitate the examination of the difficult cases

previously mentioned. These alterations have been accomplished in such a manner that the new instruments may be employed regularly by those physicians using the original instruments, without changing the technique they are in the habit of using.

The angle of the auxiliary tube with relation to the main tube has been altered by elevating it externally in order to permit the passage of the smaller instrument through the larger one, and also to provide a projecting metal surface medially to protect the glass tip which closes the distal end of the auxiliary tube. Externally, the distal end of the auxiliary tube presents a rather flat, smooth surface, so slightly elevated above the surface of the sigmoidoscope proper that it will cause no more discomfort while being inserted than did the original instrument. Changes in the smaller instrument have been confined to the proximal end. The disc at the proximal end has been provided with a collar so slotted on either side that it will engage and, with a slight "arrow-indicated" rotation, lock on two pins which project from the external surface of the sigmoidoscope proper. The handle of the obturator of the smaller instrument has been lengthened to allow the distal end of the obturator to be engaged in the lumen in that portion of the bowel examined with the larger instrument, and this engaged position is maintained until the larger sigmoidoscope has been withdrawn 3 or 4 inches, after which the withdrawal of the

larger instrument can be completed with little danger of altering the position of the smaller one. The collar on the light carrier

since constant contact with the field will tend to provide a continuous observation, rather than an observation interrupted by

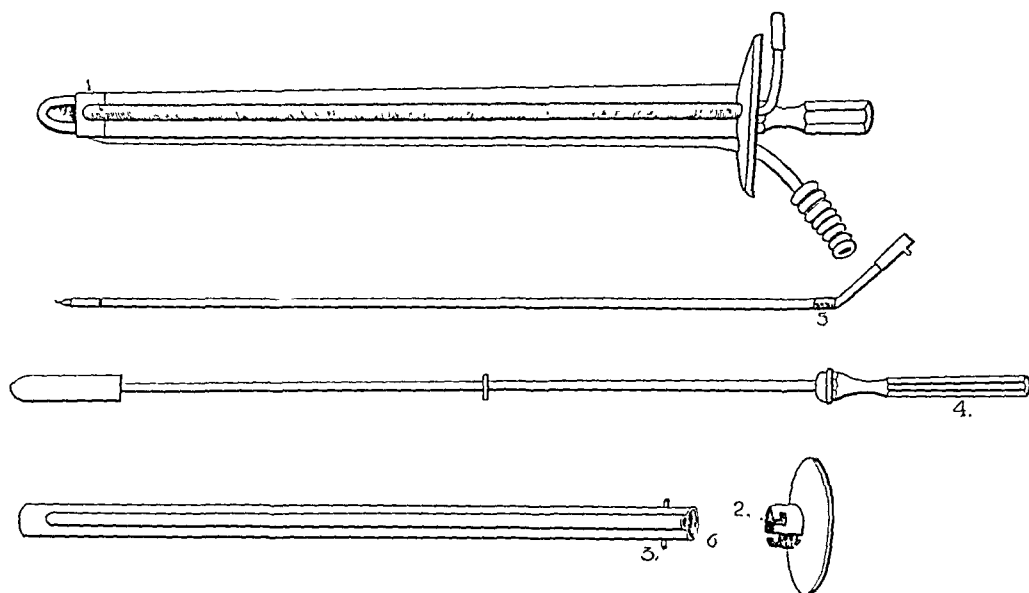


FIG. 1. Illustrates the alterations in two types of the Buie sigmoidoscope as follows: (1) distal end of the auxiliary tube, the entire tube being elevated externally both to protect glass tip at distal end and to permit passage of the smaller instrument through the larger one; (2) collar of the disc on the proximal end, with slots which engage (3) the two pins on the external surface of the sigmoidoscope proper; (4) obturator used in the smaller Buie sigmoidoscope showing how the handle has been lengthened; (5) light carrier of the smaller Buie sigmoidoscope, showing the lengthened collar which serves to prevent motion of the proximal part of the instrument during use; also, alteration in external diameter of collar to provide an airtight joint at the disc.

for the smaller instrument has been lengthened, and its external diameter has been altered sufficiently to permit it to fit snugly into the auxiliary tube, providing an airtight joint. The collar also engages the opening through the disc, preventing undue motion of this portion of the instrument during its use.

As soon as the physician is familiar with the use of the instruments, it seems reasonable to assume that these changes will enable him to examine difficult cases without the unnecessary expenditure of time and without causing unnecessary discomfort. It is also possible that the difficult examination will prove more valuable,

the complete removal of one instrument and the reinsertion of another. Two types of the larger sigmoidoscope have been designed: one with a suction tube for removing smoke during fulguration, and the other without suction. All the accessories: inflation bulb, observoscope and magnifying lens, which were designed for the original instruments, can be used in the new instruments.

Undoubtedly, these instruments will facilitate other measures, such as placing radium applications accurately at the proximal end of annular carcinomas in the rectum, rectosigmoid and sigmoid, as suggested by Dr. H. H. Bowing.



# THE USE OF A TOOL JIG AND A NEW TYPE OF SCREW IN BONE PLATING\*

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THE idea that internal bone fixation by plates or other material can be done only by a well organized group, with many specialized instruments is held in many quarters. This is not always possible, however, because transportation over long distances is not advisable in some cases. It has been the thought of the authors to simplify as much as possible the handling of some of the parts used in this type of work.

We are using a different type of screw. (Fig. 1.) It will be noted that it is a straight non-tapering type of screw without the usual tap end. We use a regular tap for threading the holes in the bone, feeling that there is less chance of the screw becoming loosened. However, the most important change is in the head of the screw. This has not the usual slot for the screw driver, but in its stead a hexagonal hole which is fairly deep. Into this hole fits a perfectly adapted hexagonal driver or wrench. The fit is so close that when the wrench is put into the screw-head the latter will not fall out. This combination of hexagonal hole and wrench has the advantage that once they are engaged there is no slipping out, both moving as one solid unit when being driven into the bone.

There is also the added advantage that loose muscle fibers or fascia cannot become entwined in the slot in the screw nor in the screw driver, since the screw margin in the head is smooth and the wrench action is at the very center of the screw with nothing overhanging the screw edge as in the case of some special screw holders now being used. We have also added a refinement in that the hexagonal wrench is fitted into a

"Yankee" type of handle, by means of which up and down strokes on the handle impart a rotary motion in either direction to the wrench.

Another device in simplifying our procedures is a tool "jig" by means of which we are able to accomplish mechanical accuracy in fitting the hole, the taps and the screws to each other. For each size screw used we have a separate "jig," one of which is shown in Figure 2 completely loaded with drills, taps and the new screws already described above. These "jigs" are turned down on a lathe from 3 inch brass solid stock. The base is of the original 3 inch stock and the neck the part turned down on a lathe; the whole comprises a solid unit. The top of the neck has three holes of equal size to hold the drills. In the shelving part of the base are three holes of the same size and threaded to hold the taps. Around the side of the base are eight holes of the same size, threaded to hold eight screws. Each "jig" is loaded previous to sterilization, wrapped in gauze and then sterilized, and is delivered on the surgeon's work table in this fashion. Each "jig" is a complete working unit; the drills will make the exact hole for the right tap, which in turn will make the exact threads for the right screw. These "jigs" can be made in any other form or shape or they may even be combined all in one unit, depending upon the desire of the individual surgeon. The chief idea is that the whole set-up is loaded previous to sterilization (even the day before, or kept always loaded) and the layout is orderly according to size. At a glance all tools and screws can be ac-

\* From the Surgical Service, Kings County Hospital.



counted for. For further simplification the hexagonal holes in the screw heads are of the same size for all size screws so that one wrench fits them all.

have found that there was a minimum of handling and picking out of small parts of the necessary armamentarium during the operation. The new type of screw seems

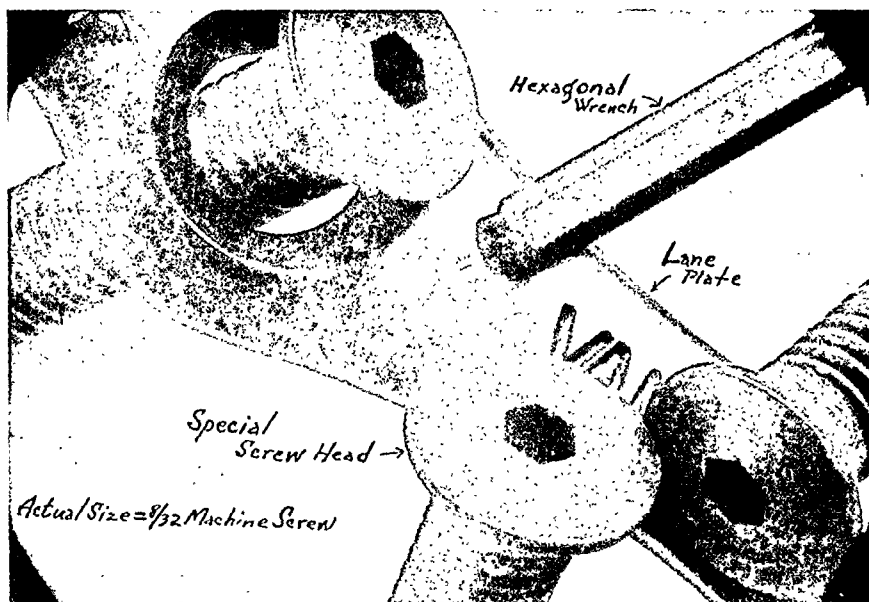


FIG. 1. Detail view of heads of screws, wrench and portion of Lane plate.

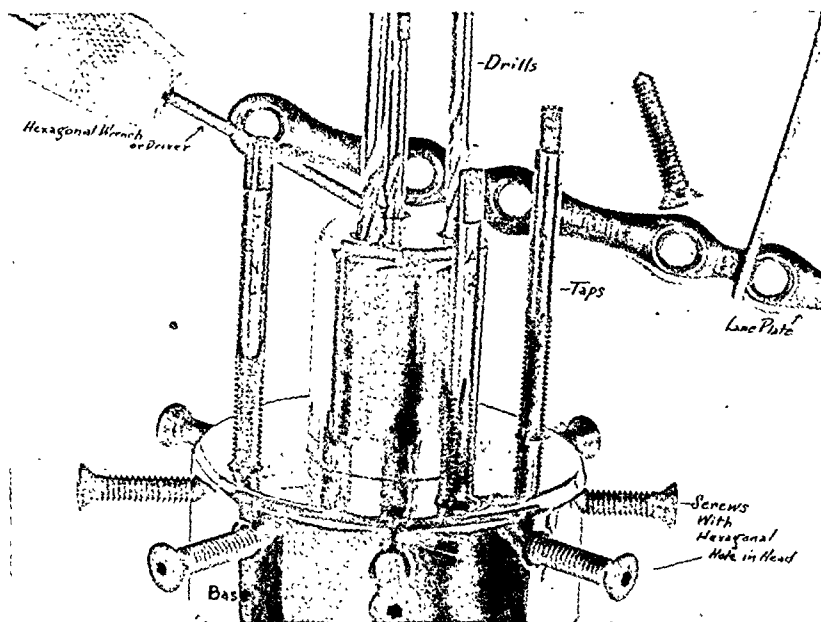


FIG. 2. Tool jig loaded with drills, taps and special screws.

We have used this set-up on the Surgical Service of the Kings County Hospital and much easier to handle in the wound than the old type.

# A BUTTON FOR HOLDING TENSION SUTURES

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TO the layman, the appearance of a scar in the skin is frequently taken as a criterion for the quality of the surgical work which has been done beneath the skin. For this reason it is important that the surgeon secure the neatest appearing scar which is compatible with efficient, rapid work. In surgery of the breast, particularly after radical mastectomy, scars, because of their ugliness, are often a source of annoyance to the patient and of discredit to the surgeon. In this area, as in many others, tension sutures are inserted and drawn so tightly that either normal bodily movements or postoperative edema cause them to cut into the skin. This helps to produce an objectionable scar. Lister<sup>1</sup> realized this and attempted to overcome it by the use of "suture buttons," made of oval pieces of sheet lead. Solid silver wire was used as suture material. A wire was wound around one button, inserted through the skin of the incision from side to side and tension maintained by wrapping the end of the wire around a second button. Interrupted sutures were also used along the skin margins. Undoubtedly the removal of these buttons was painful, and this alone helped to make them unpopular. The older textbooks of surgery—Gerster,<sup>2</sup> Pick<sup>3</sup>—mention Lister's buttons briefly, but their use is not stressed in modern English and American surgical texts. However, some surgeons at the present time are using bone buttons for the same purpose although they are a rather unsatisfactory substitute.

A modified button which we have developed is suitable for use particularly with silkworm gut. It is devoid of sharp angles and is so designed that the tension sutures may be cut and removed with a minimum of discomfort to the patient. The buttons are made of metal and, although light,

are strong enough to withstand any pull which might be exerted on them by the sutures. The holes in the buttons are large

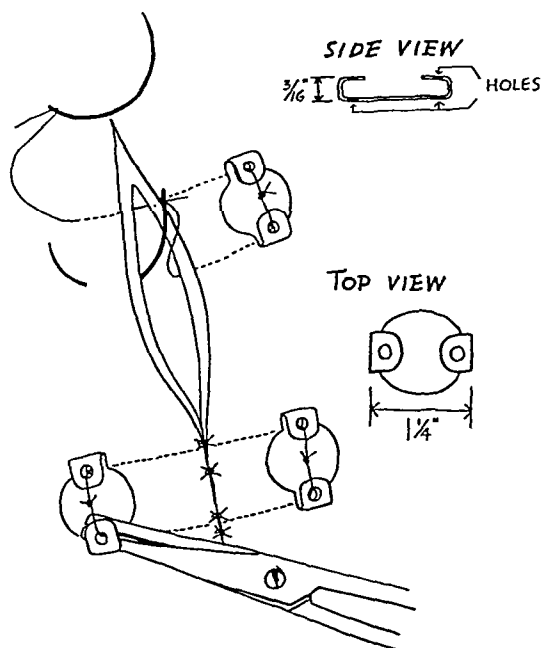


FIG. 1. Method of application and removal of tension suture buttons.

enough to allow a needle threaded with suture material to be passed through readily and when the suture is tied the button surface against the skin is large enough to allow pressure without necrosis. Figure 1 shows how the buttons are most easily applied. The ends of two sutures are tied together, one suture threaded through each half of the button, the needle and tension suture then inserted into the skin, through the incision, and out through the skin of the opposite side. The tension sutures are then threaded through a second button and the desired tension maintained when the sutures are tied together. Thus, the suture material is kept from cutting the skin. In removing the buttons, the sutures should be cut between the wing and body of the button. By doing this

a smooth end of suture material is left. There are no "hooks" of dried suture material to be pulled through the skin to the discomfort of the patient.

#### SUMMARY

A button is described for holding tension sutures in such a way that the skin is not

cut when tension is applied by means of sutures.

#### REFERENCES

1. LISTER, JOSEPH. On recent improvements in the details of antiseptic surgery. *Lancet*, 1: 787, 1875.
2. GERSTER, A. G. The Rules of Aseptic and Antiseptic Surgery, pp. 116-117. New York, 1891. D. Appleton.
3. PICK, T. P. Surgery, p. 65. New York, 1899. Longmans, Green.



STORED blood can be administered by ordinary gravity, by some form of pressure apparatus, or as a continuous drip. It must always be filtered. From—"War Wounds and Air Raid Casualties" (Lewis).

# BOOK REVIEWS

**ANAESTHESIA: NARCOSIS; LOCAL; REGIONAL; SPINAL.** By A. M. Dogliotti, M.D. Translated by Carlo S. Scuderi, M.D. Chicago, 1939. S. B. Debour. Price \$7.50.

We can recommend this book to any surgeon who wishes to add to his knowledge of anesthesia. It is replete with valuable facts and observations. The illustrations are above the average. The eleven chapters are divided into three parts, the first dealing with the historical background, pathways of sensibility and the pathologic physiology of pain, as well as the examination of the patient and preoperative care. Part 2 deals with narcosis, while Part 3 considers peripheral anesthesia. This latter section will prove valuable to the surgeon who wishes to be more familiar with regional anesthesia, spinal anesthesia, etc. This book of 680 pages from the pen of an Italian physician gives the results of his experience in this work. In translation it can now find a definite place in American literature.

**SCLEROSING THERAPY.** Edited by Frank C. Yeomans, M.D. Baltimore, 1939. Williams & Wilkins. Price \$6.00.

Although hundreds of articles on the subject of sclerosing procedures have appeared in the various surgical journals in the past five years, it is well to have a book that covers the subject in detail from every angle. This work is written by four authors and is really a series of four monographs gathered together in book form. Arthur F. Bratrud writes on The Injection Treatment of Hernia; George F. Hoch on Injection Treatment of Hydrocele; Harold J. Shelley on Injection Treatment of Varicose Veins; and Frank C. Yeomans on Injection Treatment of Hemorrhoids. The reader can, on the basis of the data presented, judge for himself the value of the technique offered.

**TEXTBOOK OF THE PRINCIPLES AND PRACTICE OF NURSING.** By Bertha Harmer, R.N., A.M. and Virginia Henderson, R.N.,

A.M. Fourth Edition. New York, 1939. Macmillan. Price \$3.00.

This widely used textbook on the principles and practice of nursing first appeared in 1922. Added editions came out in 1928 and 1934, and in this, the fourth edition, the authors have thoroughly revised the work and made it conform more nearly to the curriculum guide published by the National League of Nursing Education in 1937. A new sequence of topics has been adopted, the scope of the text enlarged and techniques included that were not in general use when the third edition was published.

The book is divided into five parts: nursing and community health service; fundamentals of nursing care; assisting with diagnostic procedures; assisting the physician with therapeutic measures; introduction to medical and surgical nursing.

This book of over a thousand pages is clearly illustrated, and the writers happily have a pleasant and entertaining style. One need give little praise to a work that has become standard and now comes to us in a fourth edition. A good, large book at a very low price.

**FUNCTIONAL DISORDERS OF THE FOOT—THEIR DIAGNOSIS AND TREATMENT.** By Frank D. Dickson, M.D., and Rex L. Diveley, M.D. Philadelphia, 1939. J. B. Lippincott Company. Price \$5.00.

This book was not written for the layman, but for the physician. It does not concern itself with pet theories, but discusses sound facts derived from personal observation and experience on the part of the authors.

Much space is given to a consideration of the foot in childhood and adolescence, for the authors feel that this period of life sees the beginning of many foot disorders. This 305 pages of text have 202 illustrations. The book is written for the understanding of the man in general practice, and is intensely practical.

It is about time that doctors of medicine knew more concerning disorders of the foot, and that the public learned to seek the physi-

cian and not a cutter of corns or a shoe salesman for the treatment of these conditions.

**THE NEUROGENIC BLADDER.** By Frederick C. McLellan, M.D. Springfield, 1939. Charles C. Thomas. Price \$4.00.

The author in this book of 206 pages has not presented original material, but has correlated the literature on the subject and presented in a readily understandable form the problem of the neurogenic bladder as a result of disease of special location in the central nervous system. This volume gives the student or diagnostician a working knowledge of the value of cystometry in the differential diagnosis of neurogenic and non-neurogenic diseases of the bladder. The appendix includes a synopsis of one hundred neurogenic bladders with pertinent data and fifty-seven figures and charts to illustrate the text. This is a worthwhile work, well presented, offering bibliography and index.

**THE PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE.** By Charles Herbert Best, M.D. and Normal Burke Taylor, M.D. Second Edition. Baltimore, 1939. Williams & Wilkins. Price \$10.00.

This unexcelled work first appeared in 1937. In two years' time it has been reprinted four times, and now appears in a new and larger edition.

The text, we are told, was written with the view of enabling the student to bring physiologic principles into more intimate relationship with the problems at the bedside. The book is long—eighty-one chapters, 1,972 pages, something for which neither authors nor publishers need apologize, for not one page could be spared. It is beautifully written and well illustrated. The references cover eighty-one pages, and the book is indexed in detail.

This is a short review, but an important, "must" book, already known as the best in its field, needs but few words to commend it.

**THE SURGERY OF INJURY AND PLASTIC REPAIR.** By Samuel Fomen, PH.D., M.D.

Baltimore, 1939. Williams & Wilkins Company. Price \$15.00.

Great strides have been made in the field of traumatic and plastic surgery during the past two decades, largely because of the increasing number of injuries due to industrial mechanization, transportation, and greater sports activity.

The author has had twenty-five years' experience in lecturing to post-graduate students and army surgeons on the subject of trauma. He divides his book into two parts, the first on general principles and the second, a regional surgery of the exterior head. The author says he intended covering the entire body, "but the impossibility of incorporating so vast an amount of material under one cover soon became apparent . . ."

The volume begins where pathologic and remedial surgery leaves off. Steps of operations are carried through to physiologic rehabilitation and anatomic restitution. Usual surgical procedures to be found in textbooks are omitted. There are about a thousand illustrations, mostly clearcut line drawings, with a great many in color.

The book is 1,409 pages long, has adequate references at the end of each chapter, and an index.

**ENDOCRINE GYNECOLOGY.** By E. C. Hamblen, M.D., F.A.C.S. Foreword by J. B. Collip, M.D. Springfield, 1939. Charles C. Thomas. Price \$5.50.

This book is for the general practitioner, and has developed from the author's lectures on endocrine gynecology. New facts in this field seem to come to light almost every month, but the author nevertheless manages to present his subject, covering the field adequately. The sections dealing with therapeutic substances and their potency will prove an aid to the general man in every day work. The cost of drugs and the values of diagnostic equipment are carefully analyzed. The illustrations (169) are excellent and different, some being in color. The book is 453 pages long, has references at the end of chapters, and subject and author indices.

SPECIAL MONOGRAPH

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PLACENTA PREVIA  
Roentgen Diagnosis, Treatment,  
and a Technique for Induction  
of Premature Labor

BY

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# PLACENTA PREVIA\*

## ROENTGEN DIAGNOSIS, TREATMENT, AND A TECHNIQUE FOR INDUCTION OF PREMATURE LABOR

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ONE of the most brilliant achievements in modern obstetrics has been the significant reduction in maternal and fetal mortality from placenta previa. The sense of helplessness which this tragic and little understood condition inspired in accoucheurs of a past age, who had no adequate weapons or knowledge with which to handle it, has given place to a spirit of confidence as new avenues of approach have been found to a solution of the difficulties that formerly seemed insuperable in its management.

This brighter outlook for placenta previa has been brought about in part by the discovery of means for its prompt and exact diagnosis and in part by the utilization of more effective methods of treatment, as well as improved technique in the older methods of procedure. It is evident that there is no standard and universal form of treatment applicable to all cases of placenta previa, but that according to the particular conditions in the individual case one or another type of procedure is indicated.

The main purpose of this paper is to evaluate the different modes of treatment in use today, and to present a method of inducing labor which the author has found useful in certain types of cases, as well as applicable in some instances of placenta previa.

### HISTORY AND LITERATURE

Placenta previa was already known to Hippocrates, who wrote: "The afterbirth should come forth last, for if it come first, the child cannot live, because he takes his life from it, as a plant does from earth. . . . When the afterbirth comes first, the child remaining within, loses its respiration and nourishment, without which it cannot live."

\* From the Department of Obstetrics and Gynecology, Sydenham Hospital, New York City.

Early writers, however, supposed that the placenta had accidentally changed its position during pregnancy from a site higher up within the uterus to a position in the uterine os. In the middle of the last century Read wrote a graphic account of the attitude taken by accoucheurs of the seventeenth and eighteenth centuries towards placenta previa.

Between 1664 and 1671 Portal reported four cases that were quite evidently placenta previa. In the first, he "separated the placenta from the internal os, to which it adhered." In another he "felt the after-burthen fastened quite round the circumference of the orifice," thus proving that he knew the placenta was attached there when found. But Van Deventer in 1734 still wrote of the "falling of the placenta" and of the flooding that it causes. In 1730 Edward Brunner wrote a thesis on "The Insertion of the Placenta over the Internal Orifice of the Uterus." Four years later William Giffard, in a treatise on midwifery, recorded many cases of placenta previa, but he too referred to the placenta as having "sunk down to the mouth of the womb."

The first record of version to stop hemorrhage of placenta previa was published by William Smellie in 1743. This author stated that he "delivered the child by the feet and so prevented the placenta from coming down first."

Mauriceau (1752) recorded his belief that when the placenta presents, it is always wholly detached, and that it acts as a foreign body which should immediately be brought away. In 1753, Wessel differentiated central and lateral insertion of a placenta previa and insisted upon rupture of the membranes before partial separation of the placenta occurred.

Levret, in his "Art des Accouchemens" (1753), wrote a chapter "to prove that the placenta may be situated on the os uteri without having been previously separated from some other part and pushed down there."

In 1775, Rigby published his classic "Essay upon Uterine Haemorrhage," in which he divided such bleedings into "accidental" (abruptio placenta) and "unavoidable" (placenta previa). As a result of several dissections, he was convinced that there must be a partial separation of the membrane in the space between the placenta and the os uteri to allow of the discharge of blood into the vagina, but that a separation of the membranes such as would admit of the

placenta's falling down could never take place before delivery of the child.

Rigby's view was soon universally accepted, and the literature of the subject since his day has been concerned chiefly with methods for early diagnosis and for prevention of these "unavoidable" hemorrhages which destroy so many lives.

Writing in 1837, Renton reviewed the subject and stated: "No person can have the slightest difficulty in believing that Portal, in 1683, knew as much on the subject of uterine hemorrhage, occasioned by the displacement of the placenta from the *os uteri*, and the practice necessary for its suppression, as we do at the present time. It is to him unquestionably that we are indebted for our knowledge on the subject."

#### INCIDENCE

The figures for incidence of placenta previa are various. Stander in 1936 placed it roughly as "once in 1000 cases in private, as compared with once in 250 cases in hospital practice." Daily gives it as 1 in 115 in the Chicago Lying-in Hospital; Aldridge as 1 in 137 for the Woman's Hospital (New York); Parks as 1 in 158 for the Sloane Maternity Hospital; Vaux as 1 in 198 for the Jefferson Maternity and the Philadelphia Lying-in Hospitals; Irving as 1 in 92 for the Boston Lying-in Hospital; Danforth as 1 in 133 for Northwestern University Medical School and Evanston Hospital, while Ude, Weum and Werner record it as only 1 in 346 at the Minneapolis General Hospital.

Beck states: "True placenta previa is rare and occurs about once in every 500 obstetric patients. . . . In hospital practice, placenta previa is observed in about 0.5 to 1 per cent of all maternity admissions."

Among causes of obstetrical deaths, Daily cites figures from the United States Department of Labor for fifteen states that would reveal a mortality of 1 in 18 from placenta previa. DeLee, averaging reports from twenty different parts of the world, found a maternal mortality varying from 1 to 19 per cent, and a fetal mortality of from 10 to 80 per cent. He states, however, that such figures are very misleading because so many different factors are involved, many of which are beyond our control. Since cesarean section has become a

common procedure in placenta previa, the mortality for both mothers and babies has been significantly reduced.

#### ETIOLOGY

Nearly all authorities agree that placenta previa is the result of some defect in the endometrium resulting in faulty implantation of the placenta. Strassmann was the first to suggest that a preceding endometritis (inflammatory or atrophic changes of the endometrium) leaves a poorly vascularized bed, which causes the placenta to spread overmuch in its attempt to bring adequate nutriment to the fetus. As evidence of this excessive spreading, Morton states that "even after the placenta has located itself, it may spread out over a larger area if for some reason the soil is inadequate. It is well known that placentas from cases of placenta previa are frequently very extensive in area, though they may be quite thin."

An interesting case is described by Thompson in which a placenta previa centralis "filled out the entire uterine segment like a cup."

Strassmann's explanation is rather generally accepted today. Davis, however, suggests it is more probable that abnormal factors in transportation of the fertilized ovum bring it too near the internal os, but admits that we know little about such factors. However this may be, it is clear that when the placenta is attached low in the uterus, near the os, there must inevitably be changes that interfere with its attachment as the uterus increases in size and the lower uterine segment forms. The increased vascularization that necessarily results from its presence here cannot fail to impair the integrity of the tissue, making it an easy prey to lacerations and hemorrhage in the later months of pregnancy. Bland points out that bleeding is further favored by the fact that the lower uterine segment is unable to contract, and the living ligature action of the interlacing fibers of the upper segment is absent. The blood is mostly from the uterine wall, not from the detached placenta. Even a slight tear in one of the sinuses in this wall may cause uncontrollable bleeding.

#### DIAGNOSIS

Traditionally, the diagnosis of placenta previa has been made on the basis of painless uterine bleeding occurring during the last three months of pregnancy. It has been confirmed by abdomino-rectal and vaginal examination, which reveals a portion of the placenta lying over the internal os.

Within recent years, however, the Roentgen ray has been called into use in this field and has opened up new means of diagnosis that are of the greatest value.

After attempts by Menees, Miller and Holly, in 1930, to reach a diagnosis by injection of strontium iodide directly into the amniotic sac (amniography) had proved too dangerous to fetal life, Kerr and Mackay (1933) tried the introduction of an opaque substance through the os uteri, only to find that this too tended to terminate pregnancy.

The method employed by J. M. Munro Kerr (1937) is to inject 20 c.c. uroselectan B into the amniotic sac through the abdominal wall. The injection should be made on the side opposite to that to which the child's back is directed. Radiographs are taken about an hour after the injection. The placenta is demonstrated as a filling defect in the outline of the amniotic cavity. While there is no bad effect on either the mother or child, this procedure tends very definitely to induce labor.

Snow and Powell are of the opinion that Roentgen visualization of the placenta in utero is important both from a clinical as well as a theoretical point of view. In a very high percentage of cases, the placenta was demonstrated in the routine examination of the abdomen of the pregnant woman.

To Ude, Weum and Urner, however, belongs the credit of utilizing cystography effectively for the diagnosis of placenta previa. Using 40 c.c. of 12.5 per cent aqueous solution sodium iodide as an opaque medium, these workers demonstrated that in cases of normal placental implantation in which the head presents, the space between the shadow of the fetal skull and that of the bladder is very slight, amounting to scarcely more than 1 cm., since the only tissues intervening are the delicate scalp of the fetus, the walls of the lower uterine segment and bladder, and a thin fold of intervening peritoneum.

On the other hand, in placenta previa they found that the presence of the placenta in this space could usually be recognized by the image of a soft crescentic mass lying between the fetal head and the bladder, separating these two structures by a space considerably wider than normal (2-3 cm.). They noted further that the size and position of the placental mass could be made out sufficiently clearly to enable them to determine whether it was a total (central) or a partial placenta previa. If it was partial, the crescent was wider on one side than on the other. Obviously this method can be of use only

in cases in which the head presents in the lower uterine segment, and is inapplicable in transverse or breech cases.

To obtain these roentgenograms, Ude and his associates used a large-sized film with the central ray directed vertically over the lower part of the abdomen. A Bucky diaphragm and a fast technique were necessary. When these conditions were fulfilled, they found it possible to make the diagnosis with a high degree of accuracy. In their first series of thirty-five cases of abnormal uterine bleeding, fourteen showed in the roentgenogram as placenta previa, and all but one of these were corroborated at delivery.

The great advantage of this method of diagnosis lies in its safety for both mother and fetus. This is due to the fact that a correct conclusion can be reached without inviting further hemorrhage by invasion of the uterus, and without danger of infection of the genital tract. In the past, when vaginal and rectal exploration in the home were the only means available for making a diagnosis, patients were exposed to all manner of possible infection, and slight bleeding easily became profuse hemorrhage under the manipulations to which they were necessarily subjected.

The value of this method was quickly recognized, and its use spread rapidly. Beck and Light reported on seventy-one cases of bleeding in the last three months of pregnancy, in which they used the method. Seventeen of these cases were placenta previa and the diagnosis by cystogram was correct in thirteen (76.5 per cent). The authors point out, however, that its greatest value is in ruling out placenta previa with a fair degree of accuracy.

McIver took up its use in all cases of painless bleeding during pregnancy, and made a report on eight cases in which the presence of a suspected placenta previa was confirmed. Titus reported that the new method, taken in conjunction with the clinical sign of bleeding and the findings of abdominal examination, enabled him to make a diagnosis of placenta previa without resorting to vaginal examination, and that the relations of the placenta to the uterus were confirmed at cesarean section.

While conceding the usefulness of the cystogram, Davis considers that the diagnosis still rests on the findings at vaginal examination, and that the presence of placental tissue covering part or all of the uterine os is diagnostic.

It is my experience that the cystogram has definitely made diagnosis simpler and easier. Although it has not supplanted vaginal

examination, in my opinion it represents one of the most valuable contributions toward the timely recognition of placenta previa, and has already been the means of saving many lives, both maternal and fetal.

It is well, however, to point out that while a negative cystogram is usually conclusive for excluding placenta previa, in an occasional case, when the placenta overlies mainly the posterior portion of the cervix, one may obtain a negative result notwithstanding the existence of a placenta previa.

Very recently Prentiss and Tucker, in an attempt to improve the contrast medium, made studies of the same kind with air cystograms. They claim that these provide a clearer, simpler and more accurate method of delineating the bladder than any liquid opaque medium that has been tried. They confirmed the high degree of accuracy of the cystographic method of diagnosing placenta previa. Five of twenty-three patients with antepartum bleeding had placenta previa. Four of these were accurately diagnosed from air cystograms, the fifth being only "suspicious." In eighteen cases placenta previa was accurately eliminated. In a breech case the air cystogram was inconclusive, just as occurs with iopax cystograms.

*Roentgen Diagnosis of Viability.* There is another way in which roentgenography renders diagnostic aid in cases of placenta previa, in that it reveals whether the fetus has reached an age when it is viable. In determining a method of treatment, it is as important to know the approximate age of the fetus as it is to recognize the cause of the bleeding and the type of implantation of the placenta at the os. A fairly accurate conception of the age of the fetus in utero may frequently be obtained by studying the degree of bone development in the plain roentgenogram. It is possible to roentgenograph the bony system of the fetus and to determine the extent to which ossification of the bony structures has taken place. This method is more reliable than determination of age by fetal measurements, which are always subject to variations dependent on nutrition, disease, traumatism, heredity and family traits. This subject has been discussed in my monograph, "The Pelvis in Obstetrics."

Hess, in 1917, and Dorland and Hubeny, in 1926, recorded the dates of appearance of the various centers of ossification as revealed by Roentgen rays.

It thus becomes possible to determine whether a fetus is sufficiently developed to survive the ordeal of birth. On the basis of this



knowledge, one may choose a suitable method of delivery. This is a matter of utmost importance in placenta previa.

#### METHODS OF TREATMENT

It has been well said by Williams that there is no single method of treatment applicable to all cases of placenta previa, and that the accoucheur who understands how to differentiate cases will obtain the best results.

In choosing the method of delivery, it is essential to take into consideration not only the variety of placenta previa, but also whether the child is living, viable, nonviable or dead. In addition, it is important to exclude the presence of monstrosities. Many of these points may be determined by roentgenography.

In olden days, the only thought of the physician was to staunch the flow of blood as quickly as possible, by any means at hand. It was not fully known that the hemorrhage, as Greenhill points out, is always associated with the rupture of some vessels which cannot be compressed until after the uterus is emptied. The old style vaginal tamponade, with material none too clean, applied by unskilful hands and in an inadequate manner, was the first recourse, and failed to accomplish its purpose. Even though it occasionally postponed death of mother and fetus, it was followed by infection and resulted disastrously. "Watchful waiting" where bleeding was at first not profuse has resulted in many a death from sudden hemorrhage in patients not under the immediate eye of the physician, and without hospital facilities close at hand. Transfusion was unknown, and bleeding to death was only too common, with loss of both mother and fetus.

The years have brought changes in our understanding of placenta previa. We now know that except in rare cases that can be kept under constant supervision, and in which the fetus is nearly viable, a quick means must be found to empty the uterus, combined with modern supportive measures to keep up the failing strength of the mother, chief among which is replacement of blood by transfusion. Placenta previa, as Schumann says, is a lesion requiring expert management and should never be treated in the home by one inexperienced.

I shall here discuss briefly the most important methods in current use for controlling hemorrhage and emptying the uterus. These are:

1. Braxton Hicks' podalic version
2. Metreuryisis (hydrostatic dilatation of cervix by bag)
3. Rupture of membranes
4. Scalp traction forceps (Willett's forceps)
5. Cesarean section
6. Gauze tamponade or pledgets of cotton
7. Author's method.

The choice of a method depends upon various factors, including the degree of placenta previa, the viability of the fetus, the general condition of the mother, the amount of dilatation of the cervix, whether there is infection, and whether the patient is at home or in a hospital. For we must recognize that in country districts, many of these cases must perforce be cared for in the home, undesirable as this may seem. Perhaps the most important factor of all is the experience and skill of the accoucheur, his ability to make the right choice of a method and to carry it through successfully.

*Braxton Hicks' podalic version* is limited in its application to cases in which the cervix is sufficiently dilated to admit two fingers. It consists in turning the fetus within the uterus (always under an anesthetic) in such a way that a foot can be brought out and drawn down until the buttocks of the fetus serve as a tampon to stop the flow of blood from the torn vessels, by compressing the placenta against the cervix. It is a procedure requiring great skill for its correct execution, but has the advantage that it can be done within the home in cases where removal to a hospital is out of the question. Its disadvantage is that it usually results in a dead fetus. No attempt should be made to extract the fetus until dilatation is complete, and this may mean hours or even days of waiting. Some practitioners tie a weight to the infant's foot to hold the buttocks fast against the cervix. If it is clear that the child cannot live in any event, some authors, as Titus, consider version better for the mother than a cesarean operation. While this method is most applicable in partial placenta previa, where the edge is easily located, in total (central) placenta previa, it is necessary to perforate any area which can be reached most easily.

*Metreuryisis (Vorbees' bag method)* should be employed in hospital practice only. Like version, it is most applicable in partial or marginal placenta previa. The bag is of soft rubber and is collapsible. It is inserted collapsed within the cervix when there is but slight dilatation. Its action, when water is gradually introduced within it, is both

to dilate the cervix and to stimulate labor pains. As a rule, no anesthetic is necessary. The bag, which should be at least 10 cm. in diameter, is kept taut against the placenta by attaching a 1 pound weight that hangs over the foot of the bedstead. In some cases the pains do not begin for several days, and it is necessary to change the bag from one size to another every twenty-four hours until a size is reached that will complete dilatation and permit expulsion of the fetus.

*Bougies.* The use of the bougie for the general induction of premature labor was employed by Krause, who wrote a monograph on the subject in 1855. In view of the fact that Krause's original work was unavailable, it is not possible to state whether this method was employed in cases of placenta previa.

According to DeLee, Krause introduced one or two elastic solid bougies into the uterus between the membranes and the wall. In two cases in which DeLee used this method for induction other than for placenta previa, the bougie caused severe hemorrhage by encroaching upon the placenta. It is thus evident that the greatest gentleness must be employed in their insertion, and that they should never be forced within the uterus in the face of resistance. The bougies, when introduced for the induction of labor in any condition, should be of soft rubber, able to curl upon themselves. In my opinion, Krause's original method would be contraindicated in placenta previa.

I have used a small soft rubber bougie with most satisfactory results in these cases, and shall deal with this subject when describing my method of inducing premature labor. Under no circumstances, however, must dilatation be hastened by manual interference. Kerr has called such a practice "the worst of all possible methods." DeLee utters a strong warning not to do hasty extraction through a poorly dilated cervix. Even the rubber bag, if overdistended and hard, may rupture an undilated cervix if not properly handled.

To insert the bag the membranes must be ruptured, and in the total (central) variety the placenta must be perforated. Some accoucheurs insist that the bag be inserted intra-ovarially in order to afford better control of bleeding. Ekas points out that extra-ovular insertion separates the placenta farther from the uterine wall, causing more concealed bleeding. Others, including La Vake, consider that the chance of getting a live baby is greatly increased if one tampons the placenta and dilates the cervix with a bag intro-

duced extra-ovularly. In either case, the patient must be watched constantly, never being left alone for a minute. She must be delivered promptly after the dilatation is complete and the bag expelled, since there is imminent danger of further hemorrhage at this moment.

I do not favor the use of a bag, for I have found that it has a tendency to increase hemorrhage. The lower segment of the uterus contains little hemostatic or contractile tissue, and is extremely friable. The extensive vascularization caused by the presence of the placenta here makes it bleed all the more readily, even though manipulations are very gentle. The several changes that may be required from one size bag to another increase the number of manipulations and invite further damage to the tissues. When the bag is expelled, if not closely watched it may lodge within the vagina while concealed bleeding continues above it. After its use the baby must still be delivered, and the maneuvers required for this accomplishment may be more than the mother can sustain in her already exhausted condition. In some of these cases version is still necessary after expulsion of the bag.

Regarding the bag as distinctly unconservative, Bill points out that it inevitably stretches and traumatizes the placental site and may thus cause postpartum bleeding. DeLee observes that the bag sometimes displaces the baby's head and allows malpresentations and prolapse of the cord, killing the baby. Even if compression of the cord does not cause disaster, the fetus is liable to suffer some degree of asphyxia, since the head cannot be delivered until the cervix is dilated, and dilatation in haste is strictly forbidden. Adair usually rules out the use of a bag except where the "life of the fetus is already extinct or of no particular value." Davis points out various practical objections to the use of the bag in the treatment of placenta previa.

Baumm advocated the use of a goat's or other animal's bladder as a metreurynter, into which glycerin is injected after its insertion into the uterus. He used this method in some 200 general obstetrical cases (type not specified), and declared that it was effective in a large percentage of these. In addition, it was wholly without danger to the mother. Not only did the bladder act as a bougie, but by osmosis the glycerin passed through the wall of the inserted bladder into the uterine cavity, where it set up contractions, often within ten minutes, through the specific irritant effect of the glycerin upon the uterine muscles and nerves.

As a general method for induction of premature labor, Klein (1926) substituted for the metreurynter and colpeurynter (vaginal bag) a Barnes' balloon, shaped like a violin, which he introduced into the rectum. Fitting the lower rectum well, this bag, to which he gave the name *procteurynter*, went high enough to reach the region where the sacrouterine ligaments branch out around the rectum. It is at this point, nearer to the rectum than to the vagina, that the ganglionic plexuses (Frankenhäuser's ganglia) are found, and according to Klein the "procteurysis" action consists in a stimulation of these ganglia, which he regarded as the centers for uterine contractions. Right here is the point of application of the procteurynter, which is designed to bring pressure upon these ganglia. The bag, well greased and tightly rolled, is introduced into the rectum as high as it will go, great care being taken not to kink it. It is then filled with hot water (45°C.). Klein stated that it is usual to observe labor pains after three or four hours, and at most, after six to eight hours. The bag causes no pain in the rectum and no bleeding.

Klein explains the action of the procteurynter definitely as the result of the pressure it exerts upon the Frankenhäuser's ganglia. He states that it has the additional advantage of avoiding infection, speeding up the outflow of secretion and making pressure upon the portio, resulting in dilatation of the os.

The stimulation of Frankenhäuser's ganglia is a matter which I consider of such definite importance for the induction of labor that I shall return to this subject later on.

*Rupture of the membranes* is often the best procedure in cases of partial or marginal placenta previa in which the head is already engaged. This makes it possible to utilize the head as a means of tamponing the placenta. In order to use this method, it is essential to know at what point the placenta will not lie in one's path, since rupture through the placenta will precipitate more hemorrhage. Since it has become possible to recognize the site of a partial previa by means of a cystogram, it is easy, under guidance of the roentgenographic film, to determine a safe point for the puncture.

I have found this method easy and safe in some cases of placenta previa of the partial or marginal type, with head presentation and dilatation already under way. Davis points out that it has the advantage of not jeopardizing any additional treatment that may be required. It effectively puts an end to any further separation of the placenta by allowing the rigid placenta to recede along with the

lower uterine segment, and thereby halts the bleeding. It initiates labor pains and facilitates the birth of a living child, without prejudice to the welfare of the latter.

The use of *scalp traction forceps* (Willett's forceps) has gained some vogue, chiefly among the continental nations of Europe. Marshall, reading a short paper before the North of England Obstetrical and Gynaecological Society, October 26, 1934, stated that in 1925 the late J. A. Willett introduced a simple method of bringing pressure to bear on the placental site by scalp traction.

He further stated that "the knowledge of the Willett's forceps is not so widespread as might have been believed." However, this method was reintroduced independently in the Wurzburg Clinic in 1931 and has since become more generally known.

Willett proposed that the scalp of the fetus be grasped with a Museux forceps, to which was attached a string hung over a pulley, with a weight not in excess of 1 pound at its other end to exert continuous traction. This results in the fetal head's making pressure upon the placenta and the uterine lower segment, which stops the bleeding and at the same time stimulates contractions and dilates the cervix. Lesions to the scalp are said to be minimal and to heal readily, without permanent injury. This method was at first used only when the fetus was known to be dead, but by degrees it began to be applied in cases of nonviable babies, and finally, on living babies at term, who were delivered in this manner without serious injury.

In a recent report on this method, Schehl states that the technique is simple, the results good, and that in the main there is no damage to the baby. The treatment is, however, directed principally to the mother, so "an occasional dead baby is to be expected." He states, nevertheless, that the mortality of the babies was two-thirds less than for combined version. The method is of course indicated only for head presentations.

According to DeLee, the use of this technique caused a 50 per cent mortality of babies in Dr. Benaron's group, and 7 per cent mortality to mothers. DeLee considers that the method has its place, however, and is as good as version or mettreuryesis when used on the same class of cases. He suggests that an "eight-pronged vulsellum" is just as good as a special scalp traction forceps.

*Cesarean section* is relatively a newcomer among methods of handling placenta previa. According to Mackenzie, who published

statistics on 22,115 cases, its use is on the increase only in the United States. Here the records show that whereas it was employed in only 13 per cent of cases in the five-year period 1924-1928 inclusive, its use was reported in 45 per cent of cases between 1928 and 1933. The general attitude in this country is perhaps reflected in McIver's comment: "Too many sections are being done, but not too many for placenta previa."

A further statement by Mackenzie would indicate that an increase of 32 per cent in the incidence of abdominal delivery in placenta previa has been accompanied by a decrease of about 5.5 per cent in maternal mortality. There was almost no mortality in the partial or marginal varieties from cesarean section, and in each degree of previa this method gives a lower mortality than does vaginal delivery. He concludes that in general the risk for the mother and baby in placenta previa is less when delivery is terminated by cesarean section than it is following vaginal delivery.

In an analysis of 47,828 cases of placenta previa in the literature, which he divided into two groups, those before and those after 1921, Findley found that the use of cesarean section had increased from 6.07 per cent in 1922 to 15.29 per cent in 1938, while maternal mortality had been more than halved, and fell well below that from vaginal delivery. His tables showed that repeated, prolonged or complicated manipulations greatly enhanced the risks to both mother and fetus.

Aldridge and Parks, reporting on the percentage of viable babies that lived after delivery, in a series studied at the Woman's Hospital and the Sloane Maternity Hospital in New York, found this to be 67.7 per cent for vaginal delivery and 85.5 per cent for cesarean at the Woman's Hospital, and 56.8 per cent for vaginal and 93.2 per cent for cesarean delivery at the Sloane Hospital.

In a recent series of ten cases of placenta previa treated by low cesarean operation, Trillat had no maternal, and only one fetal death. In eighty-eight cesarean deliveries in placenta previa, Frey had only one maternal death. Siegel, who reported two earlier series with a maternal mortality of only 2.2 and 1.72 per cent respectively, has in his latest series of 101 cesarean operations for placenta previa had only one maternal death (0.99 per cent) and twenty-five fetal deaths (24.75 per cent).

In a very recent review of the subject, Davis states that representative statistics indicate that the gross fetal mortality in cesarean

section for placenta previa averages 15 per cent, while vaginal fetal mortality is double or triple this number. This reduction in fetal mortality constitutes one of the strongest arguments for the use of the abdominal method of delivery in placenta previa totalis (centralis) where the fetus is viable and the mother able to bear a major operation.

In all cases of total (central) placenta previa in which the child is viable and in good condition, and in which there are no contraindications, it is advisable to perform a cesarean section, preferably of low flap type, as the safest procedure for mother and baby. There is general agreement, however, that section is permissible in any case in which it appears that vaginal delivery will be accompanied by disastrous bleeding.

As a rule, infection of the vaginal tract from repeated examination under conditions not strictly aseptic is a contraindication to cesarean operation. However, there are conditions under which one should even run the risk of infection rather than let the patient die of hemorrhage and exhaustion. Contraindications are also found where the fetus is nonviable, where the shock from loss of blood is too severe, in cases of uncompensated myocarditis, toxemia or poor general condition from any cause. It is obvious, too, that in cases of contracted pelvis or of abnormal presentation, a cesarean may be the only means of delivery.

These very malpresentations are often the result of the abnormal position of the placenta, which not infrequently interferes with the proper engagement of the presenting part. Success depends largely upon a wise selection of cases and the ability of the accoucheur to choose the best type of section, and to carry out its technique with the requisite skill.

Although the majority of accoucheurs prefer a classic cesarean, on the ground that it avoids the friable tissue of the lower uterine segment, one must bear in mind, in doing such a section, that the placenta if normally implanted may be encountered in the line of incision. Thus, the specific argument for giving preference to classic cesarean in placenta previa is fallacious.

My own preference is for a low flap section, since this allows full inspection of the site of attachment of the placenta—a matter of great importance. As DeLee points out, one can see the field in plain view, and it is possible to tampon or suture the sinuses of the placental site, according to the indications. One has direct access to



the source of the bleeding, and can see precisely what needs to be done.

Aldridge and Parks, who also prefer the low incision, observed that if delivery is quick, before the lower uterine segment has time to dilate, the tissues of this segment tend to retain such hemostatic power as they possess. The avoidance of trauma is one of the greatest advantages of cesarean delivery, whereas in vaginal delivery the element of traumatism is one of the most dangerous factors for the mother.

Transfusion has become an indispensable element in all these methods of treatment. Bill, in 1927, was the first to call attention to the necessity of this emergency procedure in every case of placenta previa in which there has already been an important loss of blood. He felt that in the past there had been too great haste on the part of physicians in delivering patients with placenta previa, with too little concern for the maintenance of the mother's strength by replacement of blood loss. In his own words: "If one were to analyze critically any list of fatalities from placenta previa, he could write across a large number, 'Should not have been delivered without blood transfusion,' and of nearly all the rest, 'Should have been delivered by cesarean section.'"

By introducing this supportive treatment, Bill reduced his own maternal mortality from 11 per cent to 1.78 per cent. Since one must work fast, however, he recommended that there be a transfusion team and a team for delivery which could coöperate without loss of time. At present, such an arrangement is followed in most well-organized institutions.

The improved results in placenta previa today are due as much to this replacement of blood as to the actual delivery of the patient. No treatment is good that does not protect the patient from the shock that attends profuse hemorrhage. In every case, the patient should be typed, and a donor held in readiness, in the event of blood replacement becoming an urgent need. Many of these patients require transfusion both before and after delivery. DeLee has well said that nowadays transfusion has become our best friend in hemorrhage cases.

According to Aldridge and Parks, the outstanding fault of most treatment in the series of cases reported by them was the failure to provide adequate replacement of blood loss. When a patient is in a state of shock, no attempt to deliver her by either the vaginal or the

abdominal route should be undertaken until the loss has been replaced.

#### VALUE OF THE VAGINAL TAMPONADE

In recent years, the vaginal tamponade has been regarded with some distrust by many accoucheurs, who rightly condemn it as useless or nearly so when it is inserted without a proper technique, as frequently occurs. Ekas states that it wastes time and blood. Davis says it has fallen into complete disuse, that it has survived from a time when other means of controlling hemorrhage were not available, that it most often fails to accomplish its end of checking bleeding, and that it definitely increases the hazards of infection. Both authors refer to the common gauze pack, inserted injudiciously without any definite technique, and without a view of the cervix.

In an editorial appearing in the *Journal of Obstetrics of the British Empire* some three years ago, the statement was made that when packing was done in the home, before admission to hospital, 23.5 per cent of the patients died of sepsis, "often from a few inches of gauze." Undoubtedly, this was true. Gauze decomposes, and packing in the home is likely to be inadequate and often far from sterile.

DeLee states that packing the lower segment with gauze, for induction of premature labor, is one of his favorite methods. He does this under guidance of the fingers or in the full view provided by broad specula with the vulsellum forceps, placing a strip of gauze  $3\frac{1}{2}$  yards long and 3 inches wide snugly and evenly in the lower part of the uterus and cervical canal. However, DeLee does not recommend tamponade for placenta previa except in great emergency to stop bleeding until the choice of method of delivery can be decided upon.

In induction of labor in the earlier months of pregnancy, Taussig recognized the value of the uterocervical pack.

#### AUTHOR'S METHOD OF INDUCING LABOR

In some cases of placenta previa, the author has had striking success with his method of induction of labor, which combines the use of a small size (No. 18-20 French) soft-rubber bougie and the packing of the vagina with a chain of cotton strips. This method will

be described in detail below. Its success demands a rigorous and scrupulous technique and a clear understanding of the innervation of the uterus and surrounding regions.

In an illuminating paper published in the *Journal of Obstetrics and Gynaecology of the British Empire*, in 1933, Davis presents an excellent discussion of the subject, "The Innervation of the Uterus."

Allusion has already been made to the part played by Frankenhäuser's ganglion in stimulating labor pains. In 1867, Frankenhäuser demonstrated by animal experiments that motor fibers pass from the spinal cord to the sympathetic nerve and from this to the uterine plexus, by way of the hypogastric plexus. In addition to the fibers leading directly into the cervical ganglion, he found that a wide variety of indirect connections of the sympathetic system with the uterus is also established. He pointed out that the position of the hypogastric nerves with reference to the uterus, and the close connection of their network with the nerves of the rectum is important from a therapeutic point of view, when a means of arousing labor pains is sought.

Oertel, in 1924, stated that the topographic site of the ganglia lying around the uterus (Frankenhäuser's plexus) is important for induction of labor. Similarly, Novak asserts that, in the normal, the cervical ganglia of Frankenhäuser represent the peripheral centers for the motor functions of the uterus. "Many experiments," he says, "among which may be mentioned those made upon Frankenhäuser's ganglion, prove that nerves which excite the uterus are contained in the uterine and hypogastric plexuses, and that we may, accordingly, consider the hypogastric plexus as the exciting nerve for the uterus."

DeLee points out that Frankenhäuser's ganglion, which is ordinarily  $\frac{1}{2}$  inch wide and  $\frac{3}{4}$  inch long, grows during pregnancy to a length of 2 inches and a width of  $1\frac{1}{2}$  inches.

According to Stoeckel, the hypogastric plexus and the nervus pelvici are mutually antagonistic. Since the tracts of both meet in Frankenhäuser's ganglion, he thinks that both exciting and inhibiting influences act upon the uterus from this source. He regards the automatism of the uterus as of neuromuscular origin, and as localized not only in the great cervical ganglion of Frankenhäuser, which is reinforced by paravaginal and vaginal ganglia, but also in the intramural and subserous ganglion plexuses of the uterus. He concludes, however, that it is difficult to say to what extent neurogenous and myogenous contractions combine in labor pains.

In all events, it seems evident that the pressure which is brought to bear upon the plexuses situated behind the cervix and upper portion of the vagina is what constitutes the chief value of the metreurynter, the procteuryster and the uterovaginal pack in induction of labor in placenta previa. When the vaginal tamponade is introduced with the twofold purpose of staunching hemorrhage and inducing labor, it becomes something quite different from a blind plugging of the vaginal tract with a few gauze pads pressed against the cervix.

#### DESCRIPTION OF AUTHOR'S TECHNIQUE

The external genitals should be shaved and scrubbed in the usual manner. If induction is done for other reasons than for placenta previa, especially in the early months of pregnancy, and if the vagina is roomy and the patient coöperative, it may be scrubbed as for any other vaginal operation. However, when the vagina is small and the introitus narrow, or when the patient cannot stand the pain of scrubbing, it is filled with 4 per cent aqueous solution of mercurochrome. The mercurochrome is allowed to run out and the vagina is again flushed with it two or three times.

Anterior and posterior vaginal retractors are introduced, and the cervix is brought to view. A No. 18 to 20 French soft-rubber bougie, with a piece of tape tied at its distal end, is gently introduced into the undilated cervix.

A volsella is seldom necessary, unless exposure of the cervix is difficult. If the method is being used for placenta previa, one must avoid use of a volsella on the cervix. In other types of cases, when a volsella is indicated, the instrument is applied very slowly, the successive teeth being locked in one at a time. If this is done, the procedure will not be disturbing to the patient. Once more the os is touched up with a swab in 4 per cent mercurochrome.

The soft-rubber bougie, when introduced in the cervix, curls upon itself between the membranes and the uterine wall at the point of least resistance.

The piece of tape already attached to the free end of the bougie is now wound around the proximal end of a sterile cotton strip 15 cm. long and 2 cm. thick. With this cotton strip the vagina is packed about the cervix, and the cotton tucked tightly into each fornix.

To the distal end of the cotton strip another piece of tape is tied, which, in turn, is tied similarly to the end of the next strip.

Thus a series of cotton plugs with tape connections is made. The last section of tape is allowed to hang out of the vagina.

The cotton packing, before its insertion, is wrung out in  $\frac{1}{2}$

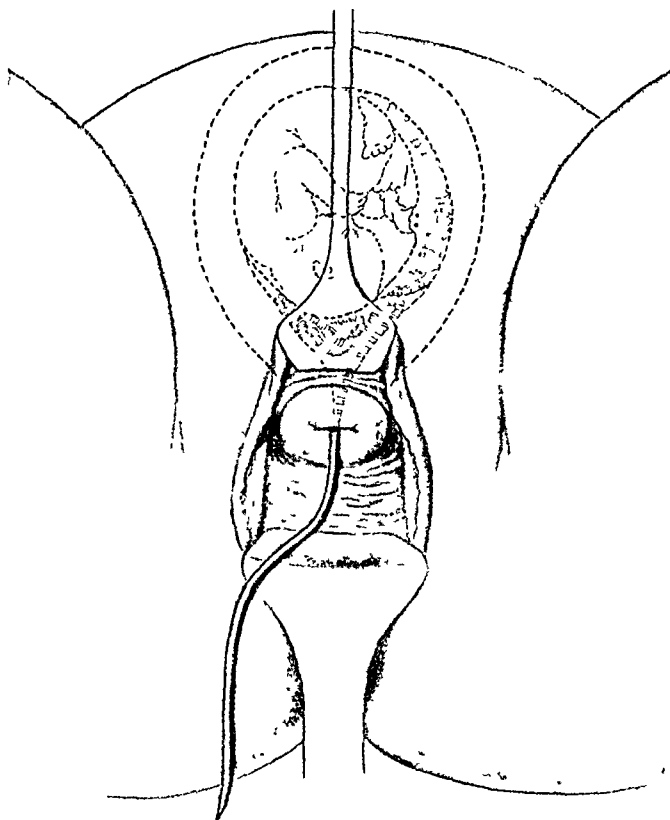


FIG. 1. Author's method of induction of labor. Anterior and posterior vaginal retractors expose cervix. Observe outline of uterus, placenta, membranes and fetus. No. 18 to 20 French, soft rubber bougie introduced into cervix. Note bougie curling in lower uterine segment indenting membranes without rupturing them.

per cent lysol solution or any other mild antiseptic, to prevent decomposition.

When the cotton strips are packed, this should be done against the blades of the retractors, in order to avoid dragging of the vaginal wall. Thus, injury to the mucous membrane as well as pain is prevented. To avoid pressure on the urethra, which may interfere with urination, the anterior retractor, when withdrawn, should be

depressed, while the packing is pressed inward with the gloved finger. By withdrawing the instrument in this manner, the pressure of the packing against the urethra is diminished and the packing will not interfere with micturition.

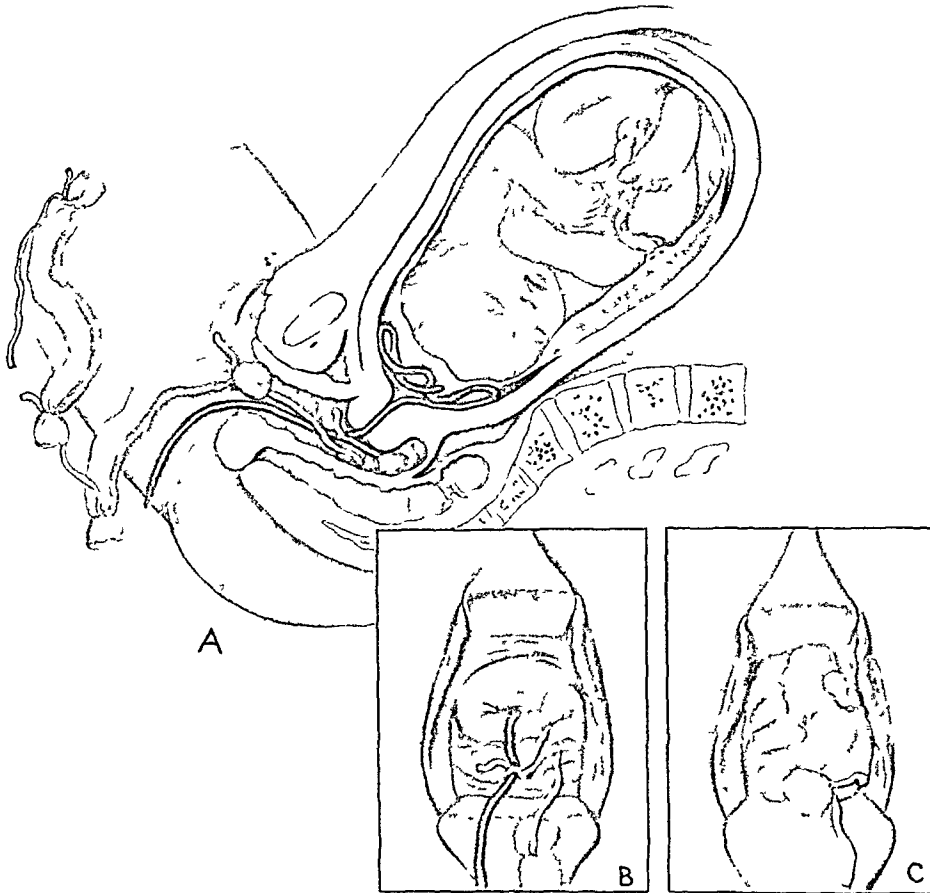


FIG. 2. Author's method of induction of labor. A, sagittal section. Observe outline of uterus, membranes, placenta and fetus. No. 18 to 20 French, soft rubber bougie introduced extraovularly into cervix. It is curled upon itself in lower uterine segment, indenting membranes without rupturing them. A piece of tape is tied to the distal end of the bougie and to the proximal end of a strip of cotton 15 cm. long, 2 cm. wide. A series of cotton strips and tape joined in this manner and arranged in a chain is wrung out in a weak lysol solution and forms a firm packing for vagina. Last piece of tape extends from vagina to insure easy removal of entire packing. B, packing of vagina. C, vagina firmly packed with successive strips of cotton. The tape attached to distal end of last strip extends from the vagina.

The packing may be left in place from twelve to seventy-two hours, provided that every twelve to twenty-four hours 4 per cent mercurochrome is injected into the vagina to prevent as far as

possible the growth of micro-organisms and decomposition in the packing. This can be done by introducing the nozzle of a glass syringe filled with mercurochrome between the strips of cotton and

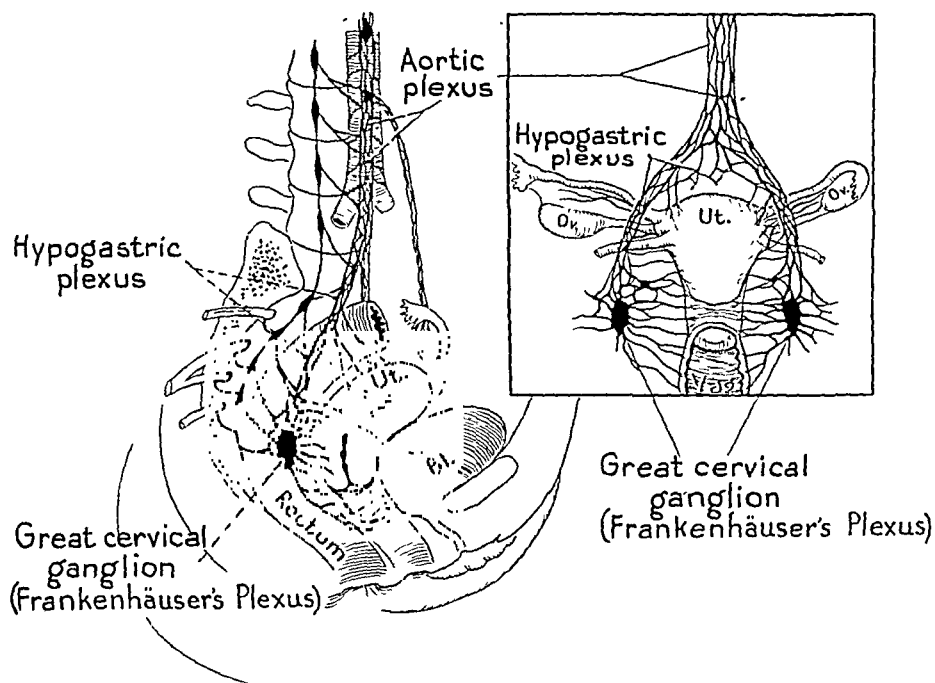


FIG. 3. The innervation of internal genitalia.

squirting the antiseptic among them, whereupon the fluid will, by capillary attraction, become distributed in the cotton strips. Furthermore, the solution, being absorbed by the cotton after the manner of a sponge, will distend the cotton packing, which will then exert greater pressure. If one desires, one may, while packing the vagina with the cotton strips, introduce a soft-rubber catheter high up within the vagina and inject the antiseptic through the catheter, so that by gravity the fluid will work its way downward and distribute itself in the packing. By using this technique, repacking becomes unnecessary.

As has already been pointed out, the effect of this vaginal packing is to make direct pressure on the great cervical ganglia of Frankenhäuser, which, coming from the hypogastric plexus, supply the uterus with its motor innervation and are thus closely associated with the induction of labor. First of all, the bougie within the cervix acts as a foreign body, stimulating these ganglia from inside the cervix. Its action is then reinforced and supplemented by the cotton

packing, which, firmly wedged into the fornices and against the cervix, furnishes a further stimulus for the setting up of uterine contractions, by its counterpressure against these important ganglia.

Labor will usually start within a few hours. Upon removal of the packing, the ovum will either follow directly or will be expelled after a brief interval. Anesthetics are seldom required during packing and only rarely during the expulsion of the ovum.

Should the patient have strong pains at the beginning of labor, at a time too early for the cervix to have dilated or for the ovum to have separated, pain may be relieved by the removal of one or two pieces of packing. This is accomplished without the use of instruments. One merely pulls at the tape and a piece of packing will be drawn out. Only in rare instances must packing be repeated. If this method is employed for placenta previa, it not only staunches the bleeding by compressing the sinuses, but also favors the induction of labor.

It should be emphasized again that when the packing is done for placenta previa, whether to control the bleeding or to induce labor, the application of the volsella to the cervix should be avoided. Also, ample time should be allowed for the presenting part to be delivered through the cervix before removing the entire chain of cotton strips. It is preferable to allow the presenting part to push out the packing. If this technique is carried out, failures are infrequent.

#### DISCUSSION

This method is particularly indicated in cases of placenta previa where there is a nonviable infant, and the placenta is centrally located. It would be the best kind of treatment, however, even in a case of this kind with a viable infant, if there are serious contraindications to cesarean section. In a case with a total (central) placenta previa and a viable fetus, in which the mother is too depleted from loss of blood to undergo a cesarean section, notwithstanding transfusion, this method should be considered until the patient recovers from shock and the choice of a method of delivery is decided upon.

The advantages of this method in placenta previa are many. It is easy and painless; it avoids shock at a time when the patient is ill able to face further shock; and it requires almost no instrumentation. It can be carried out in any country home without conveniences, where it should be of service in emergency when immediate attention is necessary.



In any case in which it is used, however, of whatever type, exactitude of technique is essential for its success. The cervix must be brought into full view, with or without use of a volsella; if the latter is employed, great importance attaches to the slow and careful use of the instrument, locking the teeth in, one at a time, to avoid laceration and pain. The same care is required in the introduction of the bougie, which should be about the size of a pencil and of soft rubber, to adapt itself to the cervical canal and lower uterine segment, into which it must be inserted with all gentleness. Once within the cervix or lower uterine segment, its action is that of a foreign body. A hard bougie is dangerous in the midst of such friable tissues, especially in placenta previa, and may increase the hemorrhage.

In packing the vagina it is not enough to make pressure upon the cervix. The cotton strips must be packed tightly into the fornices and held there by the strips lower down within the vagina which produce counterpressure. The cotton strips have the advantage over gauze in that they are easier to adapt to the vagina and as labor progresses, the strips may be removed gradually. They are superior to the separate pledgets used by some accoucheurs in that they cannot get lost within the vagina and thereby cause future trouble.

When the packing is completed, the patient can rest. If the case is one of placenta previa, there is now no bleeding, no need for haste, and the accoucheur can wait at his ease for dilatation to occur. Under supportive measures, such as transfusion, glucose in saline, and suitable medication, the patient recovers from the shock of her hemorrhage and regains strength for her delivery. However, the patient should at no time be left alone until delivery is completed and even thereafter she should be watched closely.

As a rule, the further loss of blood is negligible, and labor proceeds normally. When the pains become effective and the cervix is fully dilated, the bougie and the entire packing may be expelled together, followed quickly by the placenta, fetus and membranes, as occurred in a case here recorded. (See Figs. 6 and 7.)

#### CASE REPORTS

The following three cases are reported to illustrate how the indications may differ in individual cases. In the first, where the placenta previa was partial with a viable fetus, simple rupture of the membranes was sufficient. In the second, where the previa was

total (central) with a viable fetus and no contraindications, a cesarean section was performed at term. In the third, with a nonviable fetus and a total (central) previa, the author's method was used.



FIG. 4. Marginal placenta previa revealed by cystogram after injection of urinary bladder with 12½ per cent solution sodium iodide. Prone position. Membranes ruptured artificially. Living child obtained after thirty-six weeks of pregnancy.

CASE 1. L. M., age 37, multipara 2, was admitted to hospital November 24, 1938, at 3 P.M., complaining of vaginal bleeding of one-half hour's duration, two vulval pads being well soaked during this time. She had had no pains.

The menses had begun at 12 years, were of twenty-eight day type and seven days' duration. Her last period had been March 17, 1938. Computed date of labor was December 22, 1938.

Examination revealed a vertex presentation of the fetus in R.O.T. position; fetal heart in right lower quadrant, 140, of good quality. The head was not engaged, and the fetus was judged to be about eight months old. Blood pressure was 96/66, blood count and urine normal. A cystogram revealed the presence of a marginal placenta previa.

At 5 P.M. a vaginal examination revealed the cervix to be one finger dilated and not effaced. The fetal heart was heard in the right lower

quadrant. A piece of placenta was felt covering the posterior and right side of the os, evidently attached to the posterior and right lateral portion of the lower uterine segment and cervix. The membranes were ruptured artificially on the left side, whereupon meconium-stained liquor amnii gushed out, thus corroborating the diagnosis that the placenta was absent on the left side, but occupied the right posterior side. Thymophysin 0.12 Gm. for three doses was given every 15 minutes.

At 6 P.M. the head was fixed in the inlet, pain irregular. At 8 P.M. the pains were strong. Rectal examination revealed the head to be well engaged, the cervix three fingers dilated, and the presence of many large varicose veins of the vagina. The patient had only a few strong contractions and delivered at 8.10 P.M. a thirty-six week female baby (right occipito-anterior position). Placenta and membranes were expelled intact. There was a blood loss of 200 c.c. from the uterus and the ruptured vaginal varices. The patient did not require any blood, though a donor was prepared. She received ergotrate and 750 c.c. of 5 per cent glucose in saline intravenously. The condition of both child and mother was good. The maternal pulse was 98.

The patient ran an uneventful postpartum course except for a temperature rise to 102°F. on the first and third days postpartum. The elevation might have been due to the ligated varicose veins and iodoform vaginal packing.

*Comment.* In this case the patient had been bleeding for only one-half hour before the taking of the cystogram which revealed a marginal placenta previa on the right side. The pregnancy was known to have reached eight months; the baby was therefore viable. Vaginal examination revealed a cervix dilated to one finger, and a piece of placenta covering the posterior and right side of the os, clearly attached to the lower uterine segment and cervix. On the basis of these findings the membranes were ruptured at a safe place on the other side of the os. The patient was delivered three hours later of a thirty-six week female child. The case illustrates how the roentgenogram guides to a safe point for puncture of the membranes.

CASE II. J. W. age 34, married 7½ years, was admitted to hospital August 21, 1938, complaining of vaginal bleeding on the previous day and during the night. One normal pregnancy and labor had occurred six years previously.

The menses began at 14 years, were of twenty-eight day type and of five days' duration, moderate flow. The last menses had been January 12, 1938, and the computed date of labor was October 19, 1938.

The patient began to bleed eight weeks before term and was admitted to the hospital. A cystogram was taken and the diagnosis of total (central) placenta previa was made. After the bleeding stopped, she was kept quiet



FIG. 5. Placenta previa total (central). Menstrual age 222 days or thirty-one weeks and five days. Bladder injected with 40 c.c. 12½ per cent solution sodium iodide. Note distance of skull to shadow of bladder (over 2 cm.).

without interference. She was typed and donors were prepared for an emergency.

When she reached term, a cesarean section was done, October 19, 1938, and a living male child delivered. A centrally located placenta was found. The uterus was packed with iodoform gauze.

The postpartum course was uneventful.

*Comment.* In this case the diagnosis was made by the cystogram, which suggested a placenta previa totalis (centralis). Bleeding had begun on the day preceding admission. The exact date of conception was known. The plain roentgenogram revealed a pregnancy

of seven months, on the basis of fetal ossification. The patient was typed and donors were kept in readiness, in case of emergency. As there was no more bleeding, however, she was kept very quiet,



FIG. 6. Cystogram in case of placenta previa total (central). Apparent age of fetus six and one-half months. Note distance between fetal head and bladder shadow. Fetal skull slightly retouched.

supervised closely, and delivery was delayed until a viable child was assured. At term a cesarean was done and a live male child delivered. A total placenta previa was found, confirming the Roentgen diagnosis. The case illustrates the advantage of a cesarean operation in a case of placenta previa totalis without contraindications.

CASE III. P. F., colored, age 26, was admitted February 2, 1939, complaining of irregular lower abdominal pains and vaginal bleeding that had persisted for two days.

The menses began at 13, occurred every twenty-eight days and were of three to five days' duration, always regular and without pain. Amenorrhea had been present since birth of the patient's second child, eleven months

previously. Two previous pregnancies were both normal; no miscarriages and no abortions were reported.

One month prior to admittance the patient had had a similar attack of vaginal bleeding for two days, but without pain.

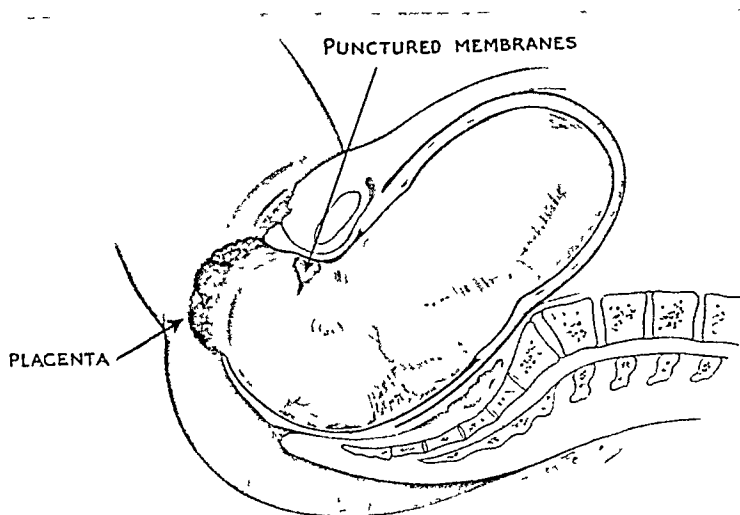


FIG. 7. Schematic drawing. Sagittal section through uterus and pelvis, showing birth of placenta followed by fetus, enveloped in membranes. Rent in anterior margin of membranes indicates site of artificial rupture.

On examination she did not appear acutely ill. The abdomen was enlarged to about a seven months' pregnancy with the fetus in the left occipito-anterior position. Fetal heart sounds were heard in left lower quadrant. The patient was spotting slightly from the vagina. Blood pressure was 120/80, the urine negative, hemoglobin 65 per cent and red blood cells numbered 3,790,000.

A cystogram showed that the distance between the head and the bladder was very wide, suggesting the presence of a centrally located placenta. The x-ray conclusion was placenta previa, central implantation.

During the taking of the cystogram a gush of blood came from the vagina and the patient began to bleed profusely without pain. The pulse rose to 120 and became thready. She was given a transfusion of 500 c.c. of blood by indirect method, followed by intravenous fluids.

A soft-rubber bougie was inserted into the cervix, together with a vaginal packing of 15 cm. long strips of cotton wrung out in  $\frac{1}{2}$  per cent lysol. Each strip was connected to the next with tape in such a manner that they formed a chain (*author's induction method of labor*). This controlled the bleeding.

About two hours later the patient began to have intermittent lower abdominal pain. Thymophysin 0.12 Gm. every thirty minutes was given for

LIGHT 2 4 39

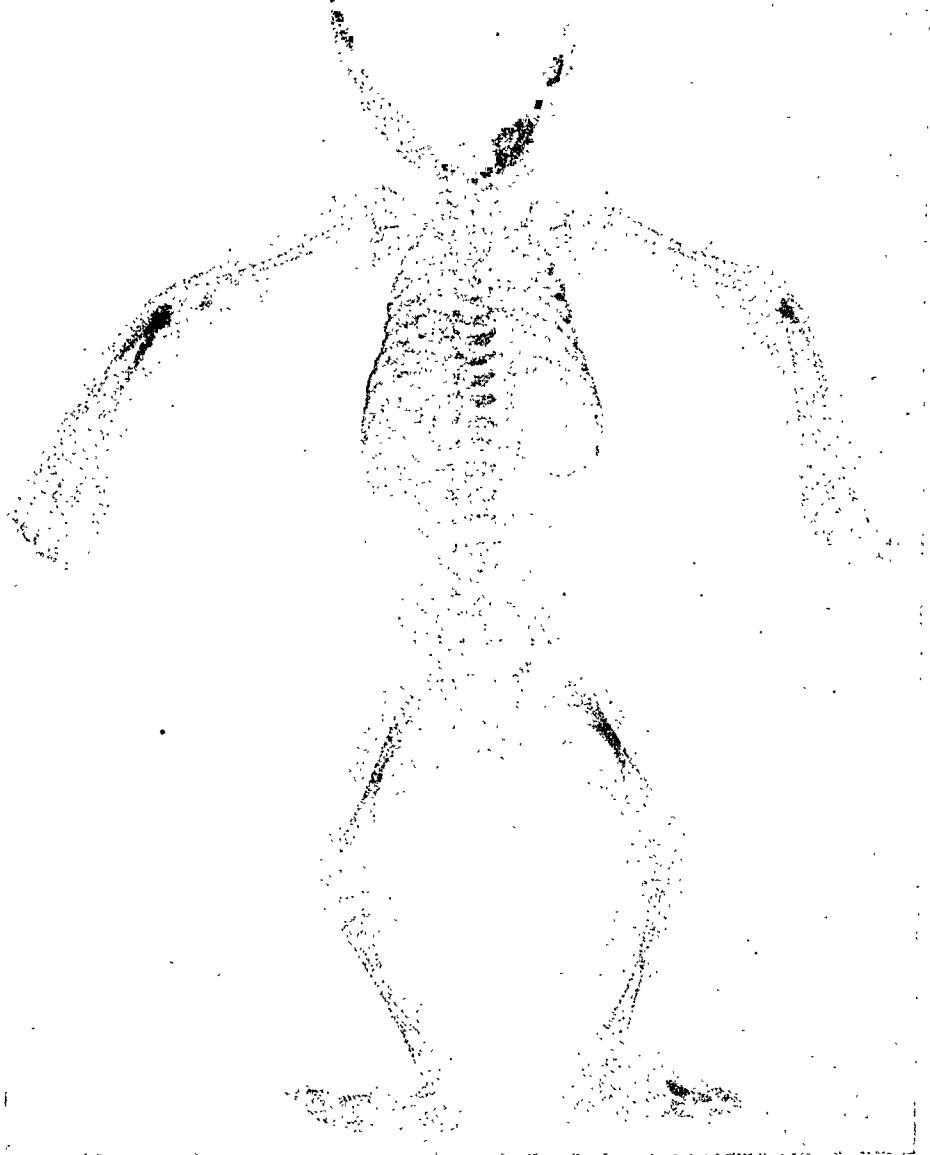


FIG. 8. Length of fetus 32.5 cm. Weight 750 Gm. Exact menstrual age not known as patient conceived two months postpartum and did not menstruate after delivery. Ossification centers of transverse processes of all lumbar vertebrae evident. Astragalus well formed; thus age is more than twenty-four weeks (between twenty-five and twenty-six), and less than twenty-eight or twenty-nine weeks, as greater cornua of hyoid bone are absent.

four doses, when the patient began to have stronger pains, followed by bearing down pains. She expelled the vaginal packing and bougie together. The placenta presented and was delivered completely before the fetus was seen. The membranes presented themselves under the pubis. A finger was insinuated under the pubis and the membranes ruptured. Labor progressed without bleeding. The entire ovum, placenta, fetus and membranes were delivered in one mass. A six and one-half months' old fetus in the sac was delivered by vertex presentation, stillborn. The blood loss throughout the procedure was not over 100 c.c. During delivery the patient was given intravenous injections of glucose in saline continuously (750 c.c.). As labor was being terminated, another transfusion of 200 c.c. of blood was given. Notwithstanding that the patient was not bleeding, the vagina was exposed and packed with iodoform gauze.

The postpartum course was uneventful, and the patient was discharged on the fourteenth day in good condition.

*Comment.* In Case III, the author's method was used successfully for induction of labor in a case of placenta previa totalis with a nonviable fetus of six and one-half months, as revealed by roentgenogram of the fetus. A study of the ossification centers from the roentgenogram of the fetus after its delivery indicated that its estimated age was correct and that it would not have survived even if delivered by cesarean section.

The patient received a transfusion before the bougie and packing were introduced, intravenous glucose in saline during delivery and a second transfusion as labor was terminated. It is worthy of note that with the exception of loss of blood when the cystogram was taken, the patient lost less blood throughout the entire procedure than occurs in a normal case, and that at its close no bleeding was present.

The method I have described for premature induction of labor is equally applicable in cases of abnormal uterine bleeding due to other causes than placenta previa, and in cases in which, for any reason, therapeutic abortion is indicated. Cases IV and V are illustrative of its use under such conditions.

CASE IV. P. T., Porto Rican, age 29, was admitted to hospital April 11, 1939, complaining of continuous vaginal bleeding and intermittent lower abdominal and back pains of varying severity since March 6, 1939. She had not noted the passing of fleshy or blood clots.

The menses began at 12 years, were of twenty-eight day type and of three days' duration. The last normal period began November 10, 1938



and amenorrhea had been present from that time until the present episode of bleeding started. She was a multipara 4, gravida 4, who had had normal and spontaneous deliveries. The last delivery had been in June, 1938.



FIG. 9 Negative cystogram in normally implanted placenta.

On admittance an elastic mass was felt, extending from the pubis to a point halfway between the umbilicus and the ensiform process. It was freely movable, nonsensitive, and contiguous with the uterus. A diagnosis of ovarian cyst was made. The x-rays showed the presence of a pregnancy of approximately five months. The Aschheim-Zondek test was positive. The diagnosis of a threatened abortion was then made. The menstrual age of the fetus was approximately 154 days. Urine and blood count were normal.

At 10 A.M. on April 18, induction of labor was done (author's method). Also, quinine hydrochloride, 3 gr., was given by mouth at hourly intervals for three hours. A soapsuds enema and an injection of pituitrin 0.12 were



FIG. 10. Negative cystogram in normally implanted placenta.

given. The pituitrin was repeated one hour later. At night the patient was given seconal, 3 gr., and slept well. On the morning of April 19, the quinine and pituitrin series was repeated. The patient complained of severe lower abdominal pains, but no definite contractions were felt. She was given rest at night by administration of seconal,  $1\frac{1}{2}$  gr. At 8 A.M. on the morning of the 20th, the patient delivered spontaneously a five months' fetus. This was forty-seven hours from the time the induction of labor was begun. An uneventful afebrile course followed and the patient was discharged eight days postpartum. The uterus was still large but firm, even at the time of her discharge. A uterine fibroid remained present.

*Comment.* In Case iv, the author's method of induction of labor was employed in a case of vaginal bleeding from a pregnant uterus, complicated by a fibroid. The woman was approximately five months' pregnant, as revealed by x-rays, and a diagnosis of threatened abortion had been made. Quinine hydrochloride and small doses of pituitrin were administered at intervals. The labor thus induced was terminated spontaneously forty-seven hours after the beginning of induction.

CASE V. R. P., age 39, a multipara 3, with one living child, was admitted May 18, 1939.

Her first menses began at 14, were of twenty-eight day type, duration five days. The last menses had occurred February 13, 1939.

The patient had a hematogenous neoplasm of the lung which had not been arrested by Roentgen therapy three years previously. She was pregnant at that time, and an induction of labor was done (author's method), because of the existing neoplasm. The patient again became pregnant against the advice of physicians, due to her eagerness for a child, and because of the fact that she had lost two of her three children. She pleaded to be allowed to carry out this pregnancy, but in view of her condition her physicians deemed it inadvisable.

On May 19, 1939, the day following admission, a soft bougie was inserted and she was packed with strips of cotton (*author's method of induction of labor*). On that day, 2 ounces of castor oil were given at 8 A.M. and 3 gr. quinine at one-hour intervals: 9, 10 and 11 A.M. A soapsuds enema was given one hour after the last dose of quinine. The patient began to have pains at 1.30 A.M. on May 21, and expelled the fetus and membranes at 2.45 A.M., approximately forty-two hours after treatment was begun.

*Comment.* In Case v, the author's method of induction was used to terminate a pregnancy for the second time, in a patient in whom a hematogenous neoplasm of the lung had not been arrested by Roentgen therapy. Notwithstanding her desire to carry out this pregnancy, she was advised by her physicians to permit its termination, in view of her unfavorable condition, due to the existing neoplasm. Labor terminated spontaneously forty-two hours after its induction was begun.

When the author's method of induction of labor is used in placenta previa, the entire packing is removed at one time, provided it is not expelled in a mass spontaneously. However, when the method is employed to terminate a pregnancy for other reasons, it may be useful to remove the strips more gradually, one fold at a

time. If the patient should have strong pains during the beginning of labor, too early for the cervix to be dilated or for the ovum to have separated, the pressure may be relieved by removal of one or two pieces of packing. This is accomplished without the use of instruments. One merely pulls at the tape and a piece of packing will be drawn out. Only in rare instances must the packing be repeated.

#### SUMMARY AND CONCLUSIONS

1. Improved means of diagnosis have made it possible to recognize placenta previa at the first bleeding, and to distinguish *partial* and *total* previas in the cystogram.
2. Roentgenographic studies will indicate the presence of monstrosities; also, the centers of ossification in the fetus reveal in advance whether it is viable.
3. The knowledge thus obtained enables the accoucheur to choose the method of treatment best suited to the individual case, without loss of time and blood.
4. The various methods of treatment are evaluated.
5. In inducing labor, the importance of stimulating the onset of labor by making direct pressure upon Frankenhäuser's great cervical ganglion is emphasized.
6. The author presents a method of inducing labor, based on this principle, and describes his technique, which he has employed for over twenty-five years, and which he believes should be considered in carefully selected cases, and in some cases of placenta previa.
7. Five illustrative cases are reported.

#### REFERENCES

- ADAIR, F. L. Discussion of Aldridge and Parks. See following reference.
- ALDRIDGE, A. H., and PARKS, T. J. End results in 400 cases of placenta previa. *Am. J. Obst. & Gynec.*, 36: 859, 1938.
- BAUMM, P. Ballonbehandlung mit tierischen Blasen. *Deutsch. med. Wchnschr.*, 39: 1201, 1913.
- BECK, A. C. *Obstetrical Practice*, 2nd Ed., p. 690. Baltimore, 1939. Williams & Wilkins.
- BECK, A. C., and LIGHT, F. P. X-ray diagnosis of placenta previa. *Am. J. Obst. & Gynec.*, 35: 1028, 1938.
- BILL, A. H. Treatment of placenta previa by prophylactic blood transfusion and cesarean section. *Am. J. Obst. & Gynec.*, 14: 523, 1927.
- BLAND, P. B., and MONTGOMERY, T. L. *Practical Obstetrics for Students and Practitioners*, 1st Ed., p. 208. Philadelphia, 1932. Davis.
- BRUNNER, E. The insertion of the placenta over the internal orifice of the uterus. Thesis, 1730.

- DAILY, E. F. Maternal deaths, a brief report of a study made in 15 states. U. S. Dept. Labor, Bureau Publication #221. Washington, D. C., 1933. Government Printing Office.
- DAILY, E. F. Placenta previa. *Surg., Gynec. & Obst.*, 59: 106, 1934.
- DANFORTH, W. C. Placenta previa. *Am. J. Surg.*, 35: 436, 1937.
- DAVIS, A. A. Innervation of uterus. *J. Obst. & Gynaec., Brit. Emp.*, 40: 481, 1933.
- DAVIS, M. E. Placenta previa. *Surg., Gynec. & Obst.*, 68: 504, 1939.
- DELEE, J. B. Principles and Practice of Obstetrics, 7th Ed., pp. 512, 522, 1028, 1165. Philadelphia, 1938. Saunders.
- DELEE, J. B. Editorial comment on Willett method. *Yearbook of Obst. & Gynec.*, 1937, p. 235.
- VAN DEVENTER, H. Observations importantes sur le manuel des accouchemens, Paris, 1734.
- DORLAND, W. A. N., and HUBENY, M. J. The X-ray in Embryology and Obstetrics. London, 1926. Kimpton.
- Editorial. Unavoidable hemorrhage. *J. Obst. & Gynaec., Brit. Emp.*, 43: 393, 1936.
- EKAS, W. L. Treatment of placenta previa by conservative measures. *New York State J. Med.*, 36: 341, 1936.
- FINDLEY, D. Management of placenta previa; analysis of 47,828 cases. *Am. J. Obst. & Gynec.*, 36: 267, 1938.
- FRANKENHÄUSER, F. Die Nerven der Gebärmutter und ihre Endigung in den glatten Muskelfasern: Ein Beitrag zur Anatomie und Gynäkologie. Jena, 1867. F. Mauke.
- FREY, E. Die Bedeutung der Lokalanästhesie für die abdominale Schnittentbindung. *Zentralbl. f. Gynäk.*, 52: 2485, 1928.
- GIFFARD, W. Cases in Midwifery, Revised and Published by Edward Hody. London, 1734.
- GREENHILL, J. P. Pathology of Pregnancy. In: Practitioners Library of Medicine & Surgery, 6: 241-399. New York, 1934. D. Appleton-Century.
- HESS, J. H. The diagnosis of the age of the fetus by use of roentgenogram. *Am. J. Dis. Child.*, 14: 397, 1917.
- HIPPOCRATES. De Morbis Mulierum, Lib. 1 (cited by Read, p. 13). See reference for William Read.
- IRVING, F. C. A study of 308 cases of placenta previa. *Am. J. Obst. & Gynec.*, 32: 36, 1936.
- JARCHO, J. Gynecological Roentgenology: A Roentgen Atlas of the Female Generative Organs with Special Reference to Uterosalphingography, p. 461. New York, 1931. Hoeber. Also *Ann. Roentgenol.*, vol. 13.
- JARCHO, J. The Pelvis in Obstetrics: A Practical Manual of Pelvimetry and Cephalometry including Chapters on Roentgenological Measurement, pp. 27, 282. New York, 1933. Hoeber.
- KERR, J. M. MUNRO. Operative Obstetrics, 4th Ed., pp. 21, 707. London, 1937. Baillière, Tindall & Cox.
- KERR, J. M. MUNRO, and MACKAY, W. G. The diagnosis of placenta praevia, with special reference to the employment of X-rays for this purpose. *Tr. Edinburgh Obst. Soc.*, pp. 21-32, 1932-1933, in *Edinburgh M. J.*, March 1933.
- KLEIN, P. Unsere Erfahrungen mit der Proktouryse. *Zentralbl. f. Gynäk.*, 50: 2493, 1926.
- LA VAKE, R. T. Hemorrhage in obstetrics. *Minnesota Med.*, 18: 4, 1935.
- LEVRET, A. L'art des accouchemens, démontré par des principes de physique et de mécanique, pour servir de base et de fondement à des leçons particulières. Paris, 1753.
- MACKENZIE, L. L. Statistical study of treatment of placenta previa. *Am. J. Obst. & Gynec.*, 33: 577, 1937.

- MARSHALL, C. H. Method in treatment of placenta previa (Report of Societies). *Brit. J. Obst. & Gynaec.*, 42: 199, 1935.
- MAURICEAU, F. The Diseases of Women with Child and in Child-bed, translated by Hugh Chamberlin. London, 1752.
- MCIVER, J. Use of the cystogram in diagnosing placenta praevia. *Texas State J. Med.*, 32: 471, 1936.
- MENEES, T. O., MILLER, J. D., and HOLLY, L. E. Amniography; preliminary report. *Am. J. Roentgenol.*, 24: 363, 1930.
- MORTON, D. G. Anatomic description of a case of marginal placenta previa, with a discussion of the etiologic implications. *Am. J. Obst. & Gynec.*, 33: 547, 1937.
- NOVAK, J. Beziehungen zu Nervensystem und Genitale. In *Biologie und Pathologie des Weibes* (Halban-Seitz), Vol. 5, p. 1394, 1924.
- OERTEL, O. Anatomie, Histologie und Topographie des weiblichen Urogenital-apparatus. In: *Biologie und Pathologie des Weibes* (Halban-Seitz), Vol. 1, p. 327, 1924.
- PARKS, T. J. See reference for Aldridge and Parks.
- PORTAL, PAUL. La pratique des accouchemens soutenue d'un grand nombre d'observations. Paris, 1685. G. Martin. Note: Quotation from English translation, author not known. London, 1705. S. Crouch & F. Taylor. (Cases 39, 41, 43 and 51.)
- PRENTISS, R. J., and TUCKER, W. W. Cystography in diagnosis of placenta previa. *Am. J. Obst. & Gynec.*, 37: 777, 1939.
- READ, W. Placenta Praevia; Its History and Treatment. Philadelphia, 1861. Lippincott.
- RENTON, R. Remarks on the literary history of uterine hemorrhage, proceeding from attachment of the placenta to the os uteri. *Edinburgh M. & S. J.*, 48: 245, 1837.
- RIGBY, E., the elder. Essay on the Uterine Haemorrhage, 1st Ed., p. 15. London, 1775. Joseph Johnson.
- SCHIEHL, E. Zur Behandlung der Placenta praevia mit der Kopfschwartenzange. *Zentralbl. f. Gynäk.*, 61: 2504, 1937. Abstr., Year Book of Obst. & Gynec., 1937, page 234.
- SCHUMANN, E. A. A Textbook of Obstetrics. Philadelphia, 1936. Saunders.
- SIEGEL, I. A. Observations on 101 cases of placenta previa delivered by abdominal Cesarean section. *Am. J. Obst. & Gynec.*, 27: 889, 1934.
- SMELLIE, W. Treatise on Midwifery. London, 1743.
- SNOW, W., and POWELL, C. B. Roentgen visualization of placenta. *Am. J. Roentgenol.*, 31: 37, 1934.
- STANDER, H. J. Williams Obstetrics. 7th Ed., p. 1109. New York, 1936. D. Appleton-Century.
- STOECKEL, W. Lehrbuch der Geburtshilfe. 5th Ed., pp. 23, 968. Jena, 1938. G. Fischer.
- STRASSMANN, P. Placenta praevia. *Arch. f. Gynäk.*, 67: 112, 1902.
- TAUSSIG, F. J. Abortion, Spontaneous and Induced: Medical and Social Aspects, p. 338. St. Louis, 1936. Mosby.
- THOMPSON, W. B. The treatment of placenta previa, together with anatomical description of two specimens. *Bull. Johns Hopkins Hosp.*, 32: 228, 1921.
- TITUS, P. The Management of Obstetric Difficulties, p. 291. St. Louis, 1937. Mosby.
- TRILLAT, P. Le shock obstétrical mortel. *Bull. Soc. d'obst. et de gynéc.*, 25: 714, 1936.
- UDE, W. H., and URNER, J. A. Roentgenologic diagnosis of placenta previa. *Minnesota Med.*, 18: 9, 1935; *Am. J. Obst. & Gynec.*, 29: 667, 1935.
- UDE, W. H., WEUM, T. W., and URNER, J. A. Roentgenologic diagnosis of placenta previa; report of case. *Am. J. Roentgenol.*, 31: 230, 1934.
- UDE, W. H., URNER, J. A., and ROBBINS, O. F. Roentgenologic diagnosis of placenta previa; indirect placentography. *Am. J. Roentgenol.*, 40: 37, 1938.
- VAUX, N. W. Discussion: See reference for Aldridge and Parks, p. 874.

- VIGNES, H., and TISSERAND, M. La méthode de Willett dans le traitement du placenta praevia. *Gynéc. et. obst.*, 35: 54, 1937. Abst., Year Book of Obst. & Gynec., 1937, p. 234.
- WESSEL, J. N. De partu cum haemorrhagia ob placentam orificio uteri adhaerentem, 1753.
- WILLETT, J. A. Method in treatment of placenta previa. Year Book of Obst. & Gynec., 1937, p. 234. See also reference for Marshall, p. 199.
- WILLIAMS, J. W. Obstetrics, 7th Ed., (revised by H. J. Stander). New York, 1936. D. Appleton-Century Co., p. 1108.

## ADDITIONAL REFERENCES\*

- CALDERA, R. Placenta praevia. *J. Obst. & Gynaec., Brit. Emp.*, 46: 531, 1939.
- PENROSE, L. S. Maternal age and parity in placenta praevia. *J. Obst. & Gynaec., Brit. Emp.*, 46: 645, 1939.

\* Appeared after preparation of this monograph was completed.

# The American Journal of Surgery

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A PRACTICAL JOURNAL BUILT ON MERIT

## EDITORIAL

### THE RISE OF THE SURGICAL MOTION PICTURE

IN spite of the policy of the various medical societies and groups to feature outstanding speakers and vital subjects at their sessions, the most liberally attended programs seem to be those where motion pictures are shown. Indeed, at the larger meetings, instead of one hall featuring a general run of surgical pictures, now three to five separate projection rooms are set up with all day programs of specialties which play to crowded houses. With the advent of color duplication in 16 mm. films and successful 16 mm. sound track on film, we are forced to pay definite attention to the future of the surgical motion picture.

The first motion picture of surgical operations on record at the American College of Surgeons is one of a cesarean section performed by Dr. Robert Fitz-Patrick in 1915. This was followed by many animated films depicting surgical technique, one of which, Kanavel's hand picture, is still a classic. In 1925 early surgical color films using the revolving wheel principle were shown in New York by Cherry and Sheehan and later a chemical process color-sound surgical film was made in Hollywood in magnacolor. Motion pictures of fluoroscopy were made first by Stewart of New York and Kawaishi of Japan in 1938. The use of the translucent screen for the showing of several slides or films simultaneously was brought out in 1939.

Realizing the importance of surgical motion pictures to audiences of mixed nationalities, the Pan-Pacific Surgical Congress at Honolulu in 1939 requested members presenting papers to illustrate them with motion pictures if possible. Special arrangements were made to preview films and aid in editing and cutting. The Association furthermore sponsored the making by me of a 1200 foot color-sound 16 mm. film on "The Making of a Surgical Motion Picture" and premiered it at the meeting. Prints of this film are now being shown in Australia and New Zealand under the auspices of the Royal Australasian College of Surgeons through the courtesy of Dr. Robert Godsall of Sydney.

It is estimated that there are over one thousand medical and surgical pictures in the United States today. Many of them are outdated or are on early color film which has now faded badly. The American College of Surgeons has an approved list of films and an exchange service for members but owns no surgical films for loan purposes. Mr. C. Carroll Adams of Davis and Geck, Inc., has built up a good library of both black and white and color films for loan to meetings, medical societies, etc. Several other companies have smaller collections of films which are available for rental or loan.

During the past twelve months the duplication of 16 mm. color film has be-



come a successful commercial venture and the reduction of 35 mm. color to 16 mm. color has also been accomplished. Sound track may now be added to 16 mm. color duplicate prints, removing the last objection to the general making of surgical movies, as the sound track can be printed on the film after it has been cut and edited.

The average charge today of the semi-professional concerns in the larger cities making surgical films, is entirely too high and is based on the premise that the surgeon knows little or nothing of how to

make a picture. However, instruction is available only by this means.

If someone were to specify, in making a bequest for the advancement of surgery, that a sum be set aside for research and help for men interested in making surgical pictures, a great good would ensue. From this, annual awards for the best films, the establishment of a general review board and a national surgical film exchange, would be natural growths. Special surgical television broadcasts are distinct possibilities for the future.

H. L. UPDEGRAFF, M.D., F.A.C.S.

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It has been called to our attention that an article on "Surface Defects of the Hand" by Dr. James Barrett Brown, published in our Emergency Surgery Symposium (December, 1939) was in large part quoted from a previous article of Dr. Brown's, published in "Annals of Surgery," June, 1938 (J. B. Lippincott and Company, Publishers). As stated in our General Information to Contributors,

"Articles are accepted for publication with the understanding that they are original contributions never previously published." This was our understanding in the present case. We deeply regret that a footnote of Dr. Brown's calling attention to the matter was unnoticed, and we present this explanation to our readers and to the J. B. Lippincott Company.

T. S. W.

# ORIGINAL ARTICLES

## THE USE OF LOCAL ANESTHESIA IN GENERAL SURGERY\*

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**M**Y first observations of operations performed with local anesthesia, chiefly hernia operations, were made during my undergraduate days. Anesthesia then consisted of desensitizing the skin, but the patient had to bear the remaining pain. As a consequence, all the patients declared that every phase of the operation had been most painful. There were some surgeons who operated without any anesthesia at all, since, in their opinion, the wound would surely become painful after the effect of the anesthesia had worn off. They considered that it would be the same to the patient whether the ache was one-half hour or longer.

In 1904, as a young intern, I was able to observe good anesthesia, as obtained by Hüttl, who employed a 1 per cent cocaine solution for minor operations. However, one of the patients died after an injection of 10 cg. of cocaine and this incident did not encourage us to undertake major operations with cocaine anesthesia.

At the same time we made a trial of Bier's lumbar anesthesia. The admirable success of the 100 cases carried out would have fixed my attention upon this procedure, if publications had not reported a mortality rate of one in 300 to 500 cases and if I had not seen the extreme post-operative suffering of the patients. Almost 30 per cent of all those operated upon developed severe headaches; in one instance I found transitory bladder palsy, in another case transitory palsy of the sciatic nerve developed.

I have made a life study of local anesthesia because of the improvement of anesthetic drugs; novocaine, tutocaine, and pontocaine. These are now applicable in larger amounts and are less toxic than cocaine, weak dilutions being effective, thus enabling their use in major operations. On the other hand, I have been deeply impressed by the horrible picture of oral operations done under general anesthesia.

Removal of buccal carcinoma, operations on the tongue or the upper and lower jaw, brought about anxiety, even if an artist, as was my first teacher Hüttl, performed them. At that time we used chloroform, later we used ether. When the patient slept deeply, we were always fearful that he might be choked by inspiring blood. When he slept superficially or woke up, the assistant, who was dressed under sterile precautions, was unable to hold the head in the position required by the operating surgeon, in order to avoid additional injury while the cautery was being used in the open mouth.

In several instances previous tracheotomy had to be performed and the orifice of the larynx had to be packed off, in order to prevent blood from flowing into the lung. Notwithstanding this, many patients died of bronchopneumonia. The patient usually began to wake up just when a major artery was spurting, so that at the end of the operation the whole field was bloody.

After a visit to Bier's clinic in Berlin and to that of Reclus at the Hôtel Dieu, I began to be troubled again with these

\* Read at a Post-Graduate Clinic Day at the Guthrie Clinic, Sayre, Pennsylvania, August 9, 1939.

questions. I could see that these horrible oral operations were transformed into uncomplicated, simple, short procedures when performed under local anesthesia, as the patient could coöperate by opening his mouth, stretching out his tongue and spitting out blood, if asked to do so.

Then I extended the field of application of local anesthesia; in 1909 I called attention to its use in abdominal operations (in *Orvosi Hetilap* and *Deutsche Zeitschrift für Chirurgie*). My present opinion is that there is no case which cannot safely be operated upon under local anesthesia. Our whole clinic is working according to this principle: general anesthesia is employed only if the procedure becomes more simple by its application, or if there is some special contraindication for local anesthesia.

The value of this method is, I think, fully illustrated by the following case: Once, when I was the professor's assistant at the Dollinger Clinic, I operated upon an old peasant, who did not utter a word during the whole operation, expecting we would anesthetize him before the procedure; when he was told that the operation was over, he would not believe it. At last he was shown his sewed wound and was asked whether he had suffered from pain. "Why, of course," he answered, "it *must* ache, if you cut a man."

Patients who have been lying in the hospital for one or two days and have watched those who have returned cheerful and relieved from the operating theater, would consider it a punishment if we attempted to anesthetize them before the operation.

I consider asepsis and anesthesia the two pillars of modern surgery. It is a well known fact that anesthesia originated in your country. (The dentist Morton and the surgeon Warren in Boston first employed ether in 1846, and the gynecologist Simpson in Edinburgh first used chloroform in 1844.) Asepsis, on the other hand, was conceived in the mind of Semmelweiss, the ingenious son of small Hungary.

Hippocrates said: "Divinum est opus sedare dolorem" (It is a divine task to relieve pain) but 2000 years later Velpeau declared that abolition of operative pain is such an absurd illusion that it should not be attempted, because there is scarcely one who has not yet suffered from it.

In common knowledge "pain" means almost the same as "disease." Pain aroused by a disease is watched most carefully by the physician, special consideration being given to its action upon the mind. Strümpell has characterized the term "pain" saying: "Pain is never caused by stimuli suitable for normal function of the organism, but it is due to some special stimulus, which disturbs the vital process of the organism and brings about such changes as never occur under physiological circumstances." We must emphasize in fact, that pain is a pathologic condition, no painful function being performed by the healthy organism. Operative pain is a highly pathologic and always a dreadful condition.

Formerly, we were almost helpless to control operative pain, as Guerin's example shows. In 1883, he proposed to burn the surroundings of the operative field by means of Viennese pasta. Dieffenbach reported a case in 1848 in which he has been unable to replace the bowels in the abdominal cavity until the patient had been made faint by letting blood from both his arms.

Though pain is undoubtedly a pathologic and dreadful condition, nevertheless it is important and is often considered a warning that the body or some organ of it is diseased. Every living being responds to changes of his bodily condition and reacts to influences that are exerted upon it by its environment. This function is fulfilled by the nervous system, which supplies all the body's members, connecting them with each other and which determines the relations between the organism and the surrounding world.

The nervous system consists of two parts: (1) the so-called autonomic (involuntary or visceral) nervous system

which regulates vital processes, as basal metabolism, blood circulation, breathing and sex functions; and (2) the central nervous system, consisting of the spinal medulla and of the brain, which brings the organism into connection with the outside world. These two parts of the nervous system form a whole, although acting differently. Certain parts of the nervous system mediate painful stimuli, others give origin to the sensation of pain.

The whole body or any part of it may be attacked by pain-causing stimuli. Inner organs may likewise undergo such painful alterations as to call the attention of the subject to the pathologic process. Pain may be started by mechanical insults, like gunshots, by cutting and stretching, by injuries caused by temperature or chemical agents or by galvanic and faradic currents. Lack of oxygen, as following arterial spasm, or vascular occlusion caused by a blood clot, may cause extreme degrees of pain.

There are receptors in almost every part of our body, picking up impulses, these being carried by sensitive fibers to the central nervous system. Each organ responds to a specific stimulus by causing the sensation of pain; thus an external hurt of the skin is painful, whereas the same injury is painless if applied to the bowel or the brain. Even the quality of pain arising from various tissues is different, since there are considerable differences in distribution and anatomy of the respective receptors.

Organs which are exposed to external influences, e.g., the skin, are more sensitive than those which are protected. There is furthermore a great difference between the sensitiveness of one individual and another; age, sex, place of residence and profession carry out a strong influence upon this matter. Northern people are more patient than southern ones; country people are more likely to suffer pain indulgently than townfolk; intelligence and strength of mind are likewise helpful in bearing pain patiently.

Pain should not be considered as a merely useful condition, protecting the organism, because its warning signal is often absent when it is important, as in beginning cancer, and often it tortures the sick in vain, especially those who suffer from incurable diseases. I readily admit that spiritual treasures have often been brought to light by bodily suffering, that it teaches us better understanding of our fellowmen and that it may allow us to look into the depths of human life, but, as seen from the point of view of the physician, *the healthy organism is free of pain*. Although pain must be endured with patience, it can never be regarded as a fundamental principle of life. Alleviation or abolition of pain is one of the most beautiful tasks of the physician.

We can achieve anesthesia today in several ways: (1) by suspending irritability of receptors; (2) by interruption of carrying impulses at some spot of the nerve trunk; (3) by anesthetizing the spinal cord we can prevent painful impressions from reaching the brain; and (4) by paralyzing the cells or a special area of the brain we may impede the subjective sense of pain from being established.

The most grateful patients may be acquired by allaying pain, for most patients judge the gravity of their disease by the pain they have to suffer. Because this does not entirely cover the facts, we must never treat pain alone, but must attempt to cure the primary disease which gives rise to the painful sensations.

Surgeons have been disputing for years whether local or general anesthesia is preferable. In my opinion, these two methods are not to be compared to each other. Most surgeons operate under local anesthesia when the patient seems incapable of standing the operation under general. Others perform operations under local anesthesia only if this method is easier.

There is a fundamental difference between these procedures; (1) in operations performed under anesthesia, the surgeon depends completely upon the anesthetist;

(2) anesthesia is a procedure which runs independently from the surgical operation and may result in death in minor as well as in serious operations. Even if we are well aware of the fact that there is but one death of each 5,000 to 10,000 cases operated upon with general anesthesia, we do not feel perfectly secure.

In local anesthesia, we must first take into account that the more efficacious an anesthetic the greater is its toxicity. In the living organism, however, toxicity of many compounds is modified under the influence of certain factors.

The diffuse speed of an aqueous solution depends on the number of molecules contained in 1 liter of the solution and on their degree of dissociation. If aqueous solutions of two different salts are put on both sides of a permeable membrane, water is pushed through the membrane until both solutions are of the same concentration. There will be an exchange of both ions and molecules until the molecular and ionic conditions are the same on both sides.

It is a further well known fact that the freezing point of water is lowest when crystalloids are dissolved in it. Aqueous solutions of the same freezing point are called isosmotic. The freezing point of blood being  $-0.56^{\circ}\text{C}$ ., every solution that freezes at  $-0.56^{\circ}\text{C}$ . is isosmotic with blood. These facts explain why injections of solutions that are isotonic with blood or tissue fluid are painless.

It must be emphasized that the absorption speed of a salt solution depends on the concentration of the solution. It is evident, however, that permeability of the tissues is a further factor in determining absorption of a certain solution. Loose adipose tissue is more permeable than thick fascia, periosteum or sheath of tendon. Absorption from the injected area will be fast or slow as to the value of local metabolism.

A chemical agent can have local effects only if it is retained in the tissue and does not enter the blood stream too quickly. The faster it enters the circulation, the more general will be its effects upon the

organism. If the drug enters the circulating blood slowly, the central nervous system receives in each moment but a small amount of the highly diluted solution and so no untoward effects need be expected.

A very remarkable point of anesthesiology is the detoxifying action of tissues upon the anesthetic fluids which have remained within their network for some time before absorption.

What is required of a good anesthetic?

1. It must be a substance capable of paralyzing the nerve tissue at a low concentration, without being a protoplasm poison to the other tissues.

2. The anesthetic should possess a specific affinity to nerve tissue. Since, if it enters the circulation, it may seriously intoxicate the central nervous system, it ought to be retained at the site of injection as long as possible.

3. The change brought about in the sensory nerve by the anesthetic must cease after a certain time without leaving a trace.

4. The anesthetic must be transformed locally by the tissues in order to be released into the circulation in a detoxified state.

5. From a surgical point of view it is important that it be water-soluble, boilable and not liable to decomposition during sterilization. It must not irritate the tissues or cause pain on injection. It must be capable of being mixed with epinephrine in order to be retained locally.

The nerves supplying the individual organs are for the most part well known, but unless they are thoroughly understood, good anesthetization is impossible.

I have been studying the question of local anesthesia for nearly thirty years. At the Surgical Clinic of Professor Dollinger, in 1904, we performed 6,000 operations under local anesthesia—95 per cent of all cases, as reported by Professor Dollinger in 1913 at the International Congress of Surgeons in London. Together with my 1,200 cases operated upon at the Zita hospital, 7,200 operations were performed under procaine anesthesia;  $\frac{1}{4}$  per cent

tutocaine was used in 6,675 cases;  $\frac{1}{2}$  per cent nupercaine in 4,420 cases; and recently pontocaine in 27,000. This makes a total of 45,295 major operations, and if I add our 41,744 operations performed upon outpatients, I can report 87,039 operations performed under local anesthesia without a single fatality during operation.

Methods have been amply commented upon in the works of Schleik, Braun, Reclus and Pauchet, I wish merely to call attention to some practical points.

The main cause of the change in anesthetics was the endeavor to use substances of the lowest possible concentration in order to depress the diffusion speed. In a major operation 180 or more c.c. of anesthetic solution is required. If a 1 per cent procaine solution is employed, this means not only the introduction of 1.5 to 1.8 Gm. of foreign substance into the organism, but also the use of a 1 per cent solution, the absorption of which, on account of its relatively high concentration, is more rapid than that of a 0.25 per cent solution (tutocaine), or of a 0.1 per cent solution (pontocaine). This will certainly increase the toxicity. That this is true, is evidenced by the fact that palpitation, pallor, diffuse sweating, rapid pulse and even nausea and vomiting during or shortly after anesthesia, were almost concomitant symptoms of 1 per cent procaine anesthesia, whereas with solutions of low concentration, the symptoms mentioned have become an extremely rare occurrence.

The anatomic site of the operation needs also careful consideration. On the head, neck or near the spinal column one cannot with impunity use as great quantities of an anesthetic as may be used far from the central nervous system, e.g., on the extremities. There the anesthetic must pass many more cells before reaching the central nervous system and in this way is more likely to be thoroughly modified or detoxified.

I would warn against injecting too great an amount at once; the dose should remain far below the toxic dose. If the patient

should feel pain during the operation, the few milligrams of the anesthetic which will have been already detoxified, permit the injection of a considerable amount of additional anesthetic solution. This continuous supplemental dosage, according to need, makes it possible to complete under local anesthesia nearly every operation started under local anesthesia. My statistics show that only 1.9 per cent of operations begun under local anesthesia had to be completed under general anesthesia.

As to methods, I have returned to, and now use extensively the Schleich, Hackenbruch and Oberst methods with the adoption of certain modifications and all methods of nerve block anesthesia, trigeminal, and cervical that Kulenkampff, Keppler, Härtel, Lāwen and others carried out endoneurally as well as perineurally. In the abdominal cavity I use the Braun anesthesia of the solar plexus, the celiac plexus, and the hypogastric plexus; infiltration of mesenteric attachments in operations on the intestine, and also parasacral anesthesia in bladder, prostate, vaginal and rectal operations. Paravertebral anesthesia I now use exclusively in kidney operations, injecting 20 c.c. of the anesthetic between the body of the twelfth dorsal and the first lumbar vertebra.

Complicated methods, in general, are likely to fail. Their drawback is that in case of failure another method has to be resorted to and this must be applicable to the operative field. I am not inclined to use spinal anesthesia, not even its modification as described by Kirschner, as long as I hear that there is one fatality in each 300 to 500 cases and that excruciating headaches are often observed.

As to the drawbacks of local anesthesia—it is said that it requires special training. This cannot be denied, but it is not a disadvantage. Moreover, in most operations the methods have been so greatly simplified that they may be easily learned.

Occasionally, a fall of blood pressure or certain toxic symptoms will occur. These, however, have become progressively more

uncommon. In any event, they cannot be compared with the more severe complications observed in general anesthesia.

It has been asserted also that some of the greater vessels may be injured. In infiltrating the deep layers I never use over-sharp needles and this makes orientation regarding the layers easier. Even if an injury occurs it will cause no serious trouble if reorganized, and if no anesthetic is injected into the vessel. In working near a vessel, if there is fear that the needle has entered, the piston is drawn back. If there is blood, the syringe is withdrawn. If the fluid is injected in such a manner that its jet precedes the needle, the stream of the fluid will drive the vessel away.

Tissue necrosis caused by anesthetics has also been described. However, I have never seen a single case of this. Those who have observed it must have infiltrated tense tissues or used great amounts of some highly concentrated fluid. Suppuration cannot be charged against local anesthesia, for both syringe and solution must be adequately sterilized.

As contraindications for infiltration anesthesia most authors mention malignant tumor, sepsis, inflammatory disease, youth, and obesity or hysteria in women. However, used far enough from the neoplasm, local anesthesia need not be feared. Moreover, operations for cancer of the tongue, cheeks, tonsils and throat have lost their bad reputation since the introduction of local anesthesia. In my opinion general anesthesia is contraindicated in septic patients. I never have seen suppuration at the site of the injection.

I never have been restrained by inflamed tissues from operating under local anesthesia and I have seen no unfortunate consequences. If the field is of small size I prefer circular infiltration in the healthy tissues, or I use block anesthesia, but if necessary, I do not refrain from infiltrating the inflamed tissue. In such cases I use a very fine needle and inject the solution slowly. In my experience, infiltration of inflamed tissues never causes spreading of

the infection; it has rather tended toward quicker amelioration or even subsidence of the inflammation, possibly by abolishing pain. I readily admit, however, that there are cases in which a superficial ethyl chloride anesthesia is to be preferred to a more complicated local anesthesia, as, for example, in extensive mastitis.

Anesthesia must be induced without pain. Methods of induction, using intravenous or other anesthetics are needless. Local anesthesia requires gentleness, patience, and anatomic knowledge. The technique is now so simple that the patient feels, even in larger operations on the stomach or gall-bladder, only one or at most two superficial needle pricks. Because of this, we have operated on a steadily increasing number of children under local anesthesia. No untoward effect from block anesthesia has been observed in either diabetic or arteriosclerotic patients.

#### SUMMARY AND CONCLUSIONS

Advantages of local anesthesia are:

1. No medical assistant is needed during operation or until the awakening of the patient.
2. General anesthesia is fraught with grave dangers, but local anesthesia can be used safely. It has great importance in fractures, since if 20 c.c. of a 0.1 per cent pontocaine solution are injected between the bone ends, pain and muscular contraction promptly cease and the fracture may be easily and painlessly reduced.
3. In general medical practice it saves a great deal of suffering. Puncture of the pleural or of the peritoneal cavity, of joints, or of a paranephritic abscess can be done without pain.

There are certain operations which I never perform under general anesthesia. In heart disease, emphysema, bronchitis, arteriosclerosis, kidney disease, in impaired liver function or in bad operative risks, general anesthesia is contraindicated. Cosmetic operations and interventions that are not absolutely necessary (removal of scars,

benign tumors), certain plastic operations, herniorrhaphies, especially umbilical hernias of fat women, I perform exclusively under local anesthesia, because I consider it inexcusable to expose the patient to the danger of general anesthesia if the same operation can be performed safely under local anesthesia. The same applies to trepanation, operations on the face, mouth, neck, thorax, and the genitourinary system.

I myself employ general anesthesia only in certain abdominal operations and in operations on the extremities if local anesthesia has proved unsatisfactory.

Postoperative pneumonia is observed in patients operated upon under local anesthesia as well as those who have had general, but it shows a more favorable course and is more easily treated.

What is still to be required of an ideal anesthetic? Painlessness is of sufficient duration for the performance of the most extensive operations. It would be desirable, however, if the operative field could be made painless for at least twenty-four hours, because after pain sensation has

returned, the patient does not breathe deeply and does not ventilate his lungs. If, however, pain could be abolished for six to eighteen hours, the patient would dare to move, to breathe deeply, and in this way many cases of pneumonia could be prevented. In this respect nupercaine opened a new perspective, but it has not fulfilled perfectly the expectations placed in it.

I am well aware that general anesthesia has changed its character, especially in America, where it has reached such a degree of perfection that its mortality rate has been reduced to a minimum and the dread of anesthesia has subsided.

Many patients prefer to be unconscious during operation and in some cases this may even be desirable, but others consider loss of consciousness unbearable and there are many cases where it is really contraindicated. From the psychologic point of view both types of anesthesia have their specific indication. General anesthesia should only be used if psychologic conditions contraindicate local anesthesia or make it impossible.





# THE CHOICE OF ANESTHESIA IN OPERATIVE PATIENTS WITH HEART DISEASE\*

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THE choice of the anesthetic to be administered to operative patients with heart disease has not always been given the careful consideration it deserves. Too often the surgeon merely determines whether he will use local, spinal, or general anesthesia without duly evaluating all the clinical factors, leaving the choice of the type of general anesthesia to the anesthetist. Not always is the state of the cardiovascular system sufficiently considered when a spinal anesthesia is chosen.

The anesthetist, though he may be an excellent technician, rarely considers the general condition of the patient, except to notice the pulse and temperature. Seldom does he take the precaution to ascertain the state of the cardiovascular system. The surgeon, on the other hand, having decided upon a general anesthetic, relies on the anesthetist to make the proper choice, and the anesthetist gives some form of inhalation anesthesia with which he considers himself most proficient.

In some hospitals progress along this line has been made. The anesthetist makes rounds on the patients to be operated upon, studies the clinical findings, and charts his recommendation as to the type of anesthetic to be used in the respective case. Should the surgeon disagree, he has the right to request the anesthetic of his (the surgeon's) choice, at the same time noting on the chart his cognizance of the anesthetist's recommendation and the reason for the desired change.

With the excellent laboratory facilities at our disposal at present, combined with our greatly enhanced knowledge of heart disease, there should be little excuse for a

death due to sudden and unexpected failure of the cardiovascular system. There are some types of heart disease so fraught with danger from any operative procedure that the risk should not be undertaken if at all avoidable. When, however, such operations become imperative it is incumbent upon the medical man to inform the surgeon of the danger, and some responsible member of the patient's family should be acquainted with the facts, and made to realize that the doctor is fully aware of the risk that must be taken. In such cases a local anesthetic is to be preferred. To avoid the risk of an unlooked for cardiac death, I have made it a practice that, except in emergencies, all patients over the age of 40 have electrocardiograms taken prior to operation. Occasionally cardiac defects are revealed which have not, or could not, be elicited by the usual physical methods. Examples are lesser degrees of A-V block, A-V nodal rhythms, bundle branch block, and qualitative and quantitative changes in the deflection comprising electrical systole which indicate disease of the myocardium. None of these can be determined with certainty except with the aid of the electrocardiograph.

The most common types of heart disease, etiologically, are: (1) rheumatic, (2) arteriosclerotic, (3) hypertensive, (4) luetic, and (5) thyroid. Frequently two or more of these types may exist in one patient.

At the outset it may be stated that the risk involved is generally directly proportional to the degree of diminution of cardiac reserve. I may illustrate with an example: Suppose a 32 year old woman enters the hospital for menorrhagia. The pelvic findings are such as to warrant hysterectomy.

\* Read before the New York Surgical Society, January 10, 1940.

But in the course of the preoperative workup a low-pitched, rumbling diastolic murmur is heard at the apex due to stenosis of the mitral valve. Further questioning reveals that the murmur has been present since the age of 10; that there have been three full term labors without difficulty; that the patient walks up three flights of stairs and does the family washing without undue dyspnea or fatigue. Obviously such a patient has little or no diminution of cardiac reserve despite the heart lesion. And clearly she is an excellent surgical risk.

At the other extreme is the case in congenital heart failure who just as obviously is a poor surgical risk. Between the two there are all gradations which can in part be determined by laboratory means, in part by physical examination by one familiar with heart disease. To the general statement made regarding the relationship of surgical risk and cardiac reserve, there are naturally many exceptions. I will try to enumerate a few of these.

In rheumatic heart disease, most frequently encountered in young individuals, one must be on the lookout for "rheumatic activity." By "activity" is meant the presence in the body of the exciting agent of rheumatic fever. In the heart, response to this agent manifests itself on the rheumatic verrucae on the valves, and the Aschoff bodies in the myocardium. "Rheumatic activity" may be determined in several ways clinically. It is sometimes manifested in the electrocardiogram by incomplete A-V block (prolonged P-R interval), or by abnormalities in the S-T segment and the T wave. Patients with acute rheumatic heart disease usually do not bear surgery well. In emergencies local or spinal anesthesia is the safest.

In the arteriosclerotic type some care must be used. These patients, of course, are not good risks per se, as the arteriosclerosis is generalized and has attacked other organs such as the liver and kidneys, has impaired their normal functions considerably, and any great strain upon their capacity can lead to disagreeable con-

sequences. Due to the impaired cardiac circulation caused by a decrease in the size of the lumen of the vessels it is best not to give anesthetics that would lessen the oxygen supply to the heart musculature. For instance, nitrous oxide would be contraindicated. Straight open mask ether would be preferable, but such anesthetics as ethylene or cyclopropaine can be used. Although cyclopropaine is being widely used today, I am not one of its unqualified advocates. There have been instances where disagreeable sequelae, such as severe respiratory complications, have been observed.

In syphilitic heart disease the nature of the lesion largely determines the risk involved. The pathologic process may be one of the following: (1) aortitis with or without dilatation or aneurysm; (2) insufficiency of the aortic valve; (3) stenosis of the coronary ostia. The first group, even when large aneurysms are present, usually stands surgery well. The last group, conversely, usually does badly, and a considerable percentage die while still on the operating table. Local anesthesia only should be used for necessary surgery. The group with aortic insufficiency is a variable one. The choice of an anesthetic in patients with this lesion depends on the duration and extent of the lesion, the amount of left ventricular hypertrophy, and degree of diminution of cardiac reserve. It should be remembered that several of the pathologic processes detailed above may be present in the same patient.

When we come to the hypertensive cases—be they the essential hypertensives, those of unknown origin, or the nephritic type—we must think more in terms of diastolic pressure than of systolic. Even with a systolic pressure well within normal limits but with a diastolic pressure of 90 or above we should be forewarned. The great danger in this type of case is anoxemia, due either to the low oxygen content of the inhaled anesthetic or to the excessive oxygen unsaturation attendant upon capillary stagnation accompanying the lowered

blood pressure of a spinal anesthetic. Nitrous oxide should not be given; avertin should be used with great care; and spinal should be looked upon as dangerous. If the diastolic pressure is near 100 or above, spinal anesthesia should be used only if directly indicated and if the advantages of its use so greatly outweigh the disadvantages that the risk must be assumed. This type of case has become so used to the high pressure, especially in the cardiac circulation, that any great lowering of pressure over a period of time, such as would be required for some major operations, may cause a sufficient anoxemia to lead to fatal results. Dr. Clarence de la Chappelle has the records of a sufficient number of such fatalities to bear out this statement. A notation on the chart stating the reason for the use of spinal anesthesia in spite of the contraindications, and in spite of the anesthetist's warnings, at the same time giving due and valid reasons for the procedure, will preclude the surgeon from being blamed for a possible mortality on the grounds of ignorance.

The thyrocardiacs are so termed because it is often difficult to say whether the heart condition is the result of thyroid disease or merely concomitant. On the other hand, quite often it can be determined that there was no heart disease per se, and that the heart lesion is the result of overstimulation as part of the general increase of body

metabolism due to thyrotoxicosis. As a rule, the latter stand anesthetics well. When we consider that we can give these highstrung persons avertin nowadays, let them go to sleep in their beds and find themselves in their bed when they wake up after a successful operation, there is really very little excuse for subjecting them to the terrific psychologic trauma of operation under local anesthesia. Most qualified authorities on thyroid surgery will use local only under exceptional circumstances when other forms of anesthesia are contraindicated. It should be stated at this time that auricular fibrillation in these cases is no contraindication to thyroidectomy. In spite of the fibrillation these patients stand operation well, and frequently the fibrillation disappears in a few days.

#### SUMMARY

1. The most common types of heart disease have been discussed from the standpoint of a choice of anesthetics.
2. Anesthetics have been chosen for each type of heart disease that will involve the least risk.
3. Contraindications to certain anesthetics in various types of heart disease have been emphasized.
4. A suggestion for the improvement of the service by a more careful consideration in the choice of anesthetics by both the surgeon and the anesthetist has been made.



# SOME MECHANICAL DERANGEMENTS OF THE KNEE AND SHOULDER\*

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THE knee joint is the largest joint in the body. Its skeletal structure is unstable, for it consists merely of the expanded ends of the femur and tibia, necessitating an ingenious and effective ligamentous system.

Derangement of the semilunar cartilages is the most common cause of intrinsic disorders of the knee joint, and the internal semilunar cartilage is the chief offender. It is estimated that it is involved four to ten times more often than the external semilunar cartilage. Because they are fibrocartilaginous in structure, the semilunar cartilages become torn in their substance rather than broken or fractured. The internal semilunar cartilage is firmly adherent to the capsule, whereas the external semilunar cartilage is loosely attached. These facts are important because, if the internal semilunar cartilage is caught between the condyle and the head of the tibia, it cannot escape, but will become ripped or torn in its substance. The external semilunar cartilage, due to its loose attachment to the capsule, has a certain amount of freedom, and thus may slip out of the grasp of the ends of the bones.

The crucial ligaments are also important. The anterior crucial ligament courses from the anterior part of the tibial platform near the tibial spine, upward, backward and lateralward to be attached to the lateral condyle of the femur. It prevents the tibia from slipping forward on the femur and prevents the femur from slipping backward on the tibia. The posterior crucial ligament arises posteriorly from the area contiguous with the tibial spine and courses upward,

forward and medialward to be attached anteriorly to the medial condyle of the femur in the intercondylar notch. It prevents the femur from slipping forward on the tibia and prevents the tibia from slipping backward on the femur. The crucial ligaments are damaged in mechanical derangements of the knee joint more often than is realized, the anterior ligament being injured more frequently than the posterior. It is possible that the pull on the crucial ligament at its attachment to the internal condyle may have something to do with the formation of loose bodies in cases of osteochondritis dissecans.

In 1934, we made a study of the records of 560 patients who were suffering from derangement of the knee joint and who were operated on at The Mayo Clinic.<sup>1</sup> There were 587 operations: 343 for derangement of the semilunar cartilage and 244 for osteocartilaginous bodies. Three hundred and thirteen operations were performed for injuries of the internal semilunar cartilage and thirty were done for injuries to the external semilunar cartilage. There were four males to one female, and most of the patients were less than 30 years of age.

## DERANGEMENT OF THE SEMILUNAR CARTILAGES

The patient is usually a male in the active period of life, and engaged in some active pursuit or sport when the injury occurs. The knee is usually in a partially flexed position with the foot externally rotated. (Fig. 1.) The pain consequent to the locking may be excruciating, there is

\* Abstract of lecture given at the University of Minnesota, Center for Continuation Study, Minneapolis, March 14, 1939.

inability to extend the knee completely and swelling occurs within a short time. Later, when ambulatory, the patient may note a

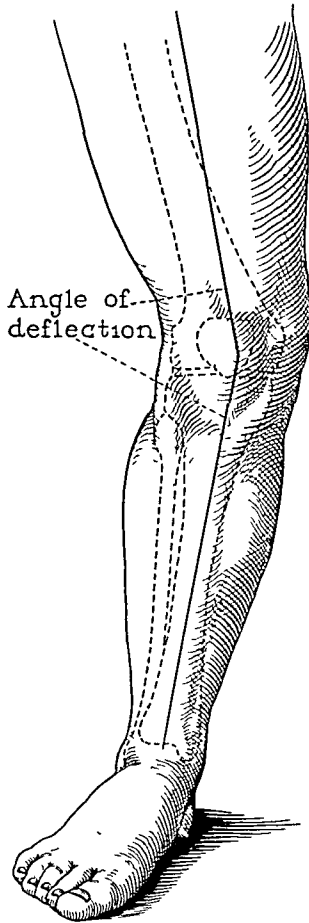


FIG. 1. Angle of weakness of knee; partial flexion with eversion of foot.

feeling of insecurity as if something were amiss in the joint. The pain is diffuse at first, but the tenderness gradually becomes localized, depending on which cartilage is involved, and the effusion gradually is absorbed. Usually, recurrent attacks of locking occur while the patient is engaged in some sport, but occasionally there is no history of injury and we have records of several cases in which locking has occurred on merely turning over in bed. The onsets tend to become more frequent as a rule, but the pain and ensuing swelling seem to lessen each time. The diagnosis rests almost entirely on the subjective symptoms, for when the patient presents himself

to the surgeon there is usually nothing abnormal to be seen or felt in the knee and study of the roentgenogram usually gives negative results.

In mild cases of arthritis some confusion may arise as there may be a sensation of catching skin to locking caused by the synovia being nipped between the joint surfaces. Complaints of symptoms from other joints should serve to put the surgeon on guard. Osteocartilaginous bodies are readily detected by roentgenologic examination, but in some cases of the early stages of osteochondritis dissecans in which the body is not yet separated, there is a feeling of insecurity and instability similar to cases in which the semilunar cartilages are at fault.

Derangement of the external semilunar cartilage causes the same symptoms as derangement of the internal cartilage except that the pain is generally referred to the outer side of the knee in the former instance.

#### OPERATION

Unless locking of the knee cannot be reduced the first time that it happens, operation should not be performed until locking of the knee has occurred several times. If, in addition to locking, the internal semilunar cartilage is injured, it is preferable to make a small, anterior, internal incision across the triangular space bounded by the tibia, the condyle of the femur, the patella and the ligament of the patella, with the knee flexed to form a right angle. (Fig. 2.) If the external semilunar cartilage is involved, the space on the outer side of the knee corresponding with that just described should be opened. It is possible to remove the entire cartilage through an anterior incision, but if, in such an endeavor, the incision must be enlarged so as to endanger the lateral ligament, it is better to remove the anterior portion of the cartilage and to make a posterior lateral incision on the inner or outer side, depending on which cartilage is to be removed, and the posterior part of the cartilage

should be removed through this separate incision. The operation should be done with a tourniquet in place and after the opera-

handle fracture described by Rutherford Morison many years ago. I think a better term would be "loop" tear, because it is in

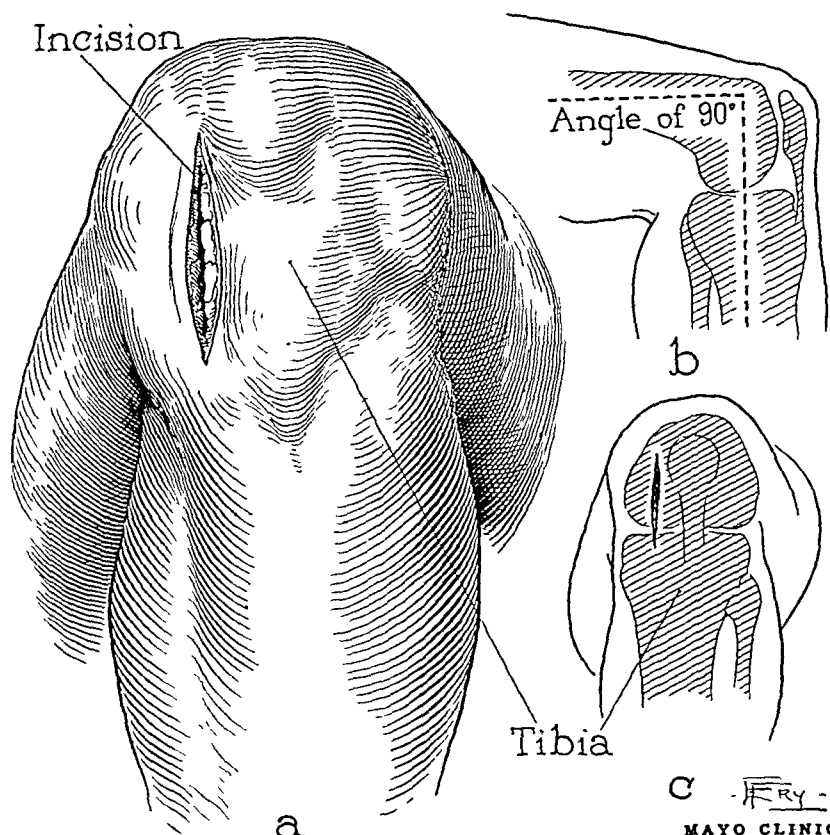


FIG. 2. Antero-internal incision for removal of internal semilunar cartilage.

tion is completed, the knee should be held for at least seventy-two hours on a posterior splint or in a plaster cast in almost complete extension.

#### PATHOLOGY

There are four types of tears or fractures which are most commonly seen in the internal semilunar cartilage. (Fig. 3.) One is a tag-like flap of the internal semilunar cartilage hanging from the anterior portion of the cartilage, which may flop back and forth and may be caught between the condyle and the tibia.

The second is also pedunculated, but arises in the middle third. If it is folded backward it may be difficult to see on opening the knee joint.

The third, and in our experience the most common, is the so-called bucket

the form of a loop, being attached anteriorly to the anterior portion of the semilunar cartilage and posteriorly to the posterior portion. The loop lies in the intercondylar notch and prevents extension of the knee.

The fourth is a pedunculated tag or flap in the posterior third. This type produces bizarre symptoms and cannot be seen through an anterior incision.

The types of tears of the external cartilage are not so constant or so readily classified as those of the internal cartilage. In our experience the bucket handle type is the most common type of tear of the external cartilage.

Of the 343 operations, there were 122 in which a fracture was not demonstrable whereas, in 221 instances a fracture or tear could be shown. Derangement may be

caused by a hypermobile cartilage which manages to slip out of the grasp of the ends of the bones before actual damage occurs.

possibility should be explained to patients before operation if any instability of the knee is present and they should be warned

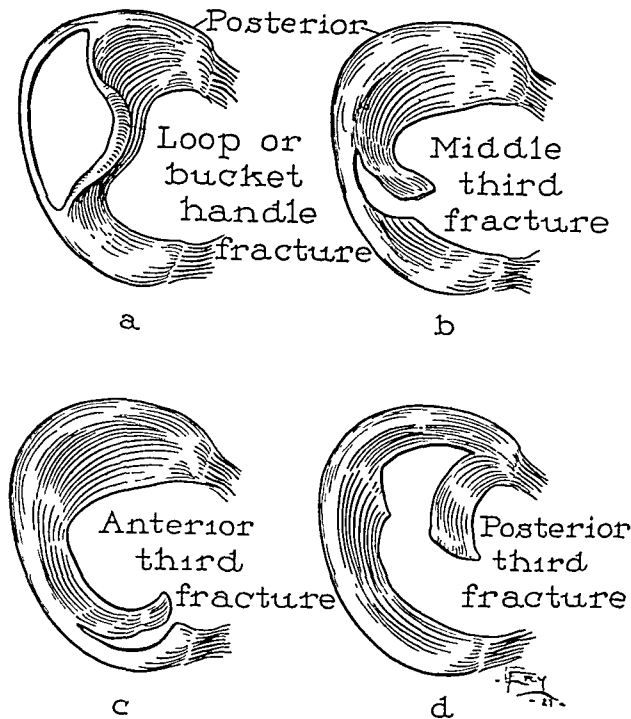


FIG. 3. Four common types of tears in internal semilunar cartilage. (From Henderson, in *S. Clin. North America*, 7: 1425, 1927.)

The symptoms are very similar to and usually cannot be distinguished from those which are present when a fractured cartilage is the cause of the disability. However, the percentage of good results among patients who had the cartilage removed because it was thought to be hypermobile is not so great as among those who had tears or fractures of the meniscus that were demonstrable at operation.

#### RESULTS

Complete relief was obtained in 77.3 per cent of the cases in which operation was performed. In addition, in another 15.3 per cent of these cases definite improvement and relief of many of the symptoms were noted. In 7.4 per cent improvement did not occur. I feel sure that in some of the cases, failure to realize relief was due to the fact that severe injury and partial rupture of the crucial ligaments had occurred. This

that, although the operation will relieve the locking or catching in the knee, if they have ligamentous injury the weakness will probably persist.

#### OSTEOCARTILAGINOUS LOOSE BODIES

Derangements due to osteocartilaginous loose bodies may be classed under three headings: first, those in which the bodies arise because of osteochondritis dissecans; second, those due to osteoarthritis; and third, those due to osteochondromatosis.

Osteochondritis dissecans and osteochondromatosis occur in young patients, whereas osteoarthritis occurs in the more elderly. In the aforementioned group study there were 233 patients, 187 males and fifty-seven females, who were operated on for the removal of loose bodies in the knee joint.

*Osteochondritis Dissecans.* One hundred and thirty-five of 233 patients had loose

bodies due to osteochondritis dissecans. (Fig. 4.) There were 105 males and thirty females. The internal condyle was the site

synovial fluid to allow formation of cartilage that will completely surround the body. In a few cases loose bodies were removed

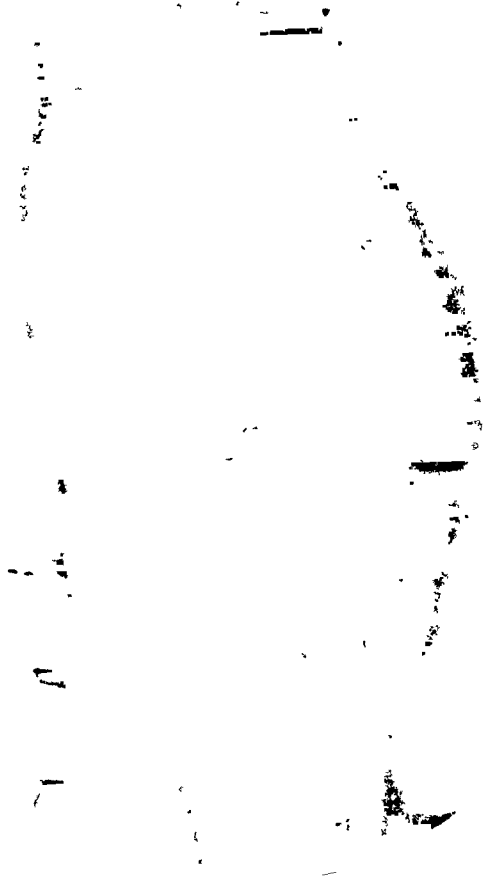


FIG. 4. Osteochondritis dissecans of the internal condyle of the femur. (From Henderson, in *South. M. J.*, 19: 633, 1926.)

of origin in 118 cases. In some cases it was impossible to determine from just what place the loose body arose, but in a few it evidently originated from the external condyle. The etiology of osteochondritis dissecans is not understood thoroughly, but it is probable that there is a blocking of an end artery with consequent aseptic necrosis of a portion of bone and cartilage, and the body is cast off and wanders about the joint. Loose bodies in cases of osteochondritis dissecans are usually single and rarely exceed two or three in number and they may be completely covered with cartilage because, as they wander about the joint, sufficient nourishment is obtained from the

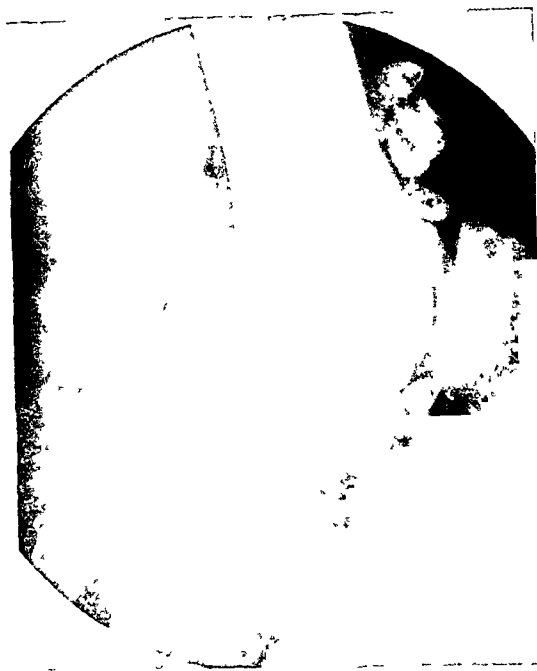


FIG. 5. Osteochondromatosis with multiple osteocartilaginous bodies.

from both knees. When the body is removed, the roughened edges about the region from which it has been derived should be smoothed down.

Some adolescent patients may have very indefinite symptoms. They may complain merely of a feeling of insecurity in the knee. There may not be much pain, but a disability may curtail activity. Later on, the body shows up on roentgenologic examination.

**Osteochondromatosis.** We believe that osteochondromatosis is a benign neoplastic process. (Fig. 5.) The bodies originate in the synovial membrane, usually at the margins where the membrane is reflected from the bone, but occasionally the entire synovial sac participates in the process. Small pedunculated tags of tissue hang down and become fibrous on the tip; then cartilage and bone actually form in them. They become broken off as they become larger and heavier, and wander about the joint. As long as these bodies are attached by a pedicle and have a blood supply, the



bone in them is alive, but on breaking free from their pedicle the bony portion becomes necrotic. The number of the bodies

catching and locking only, but will in no way help the arthritis.

Osteocartilaginous bodies vary in size

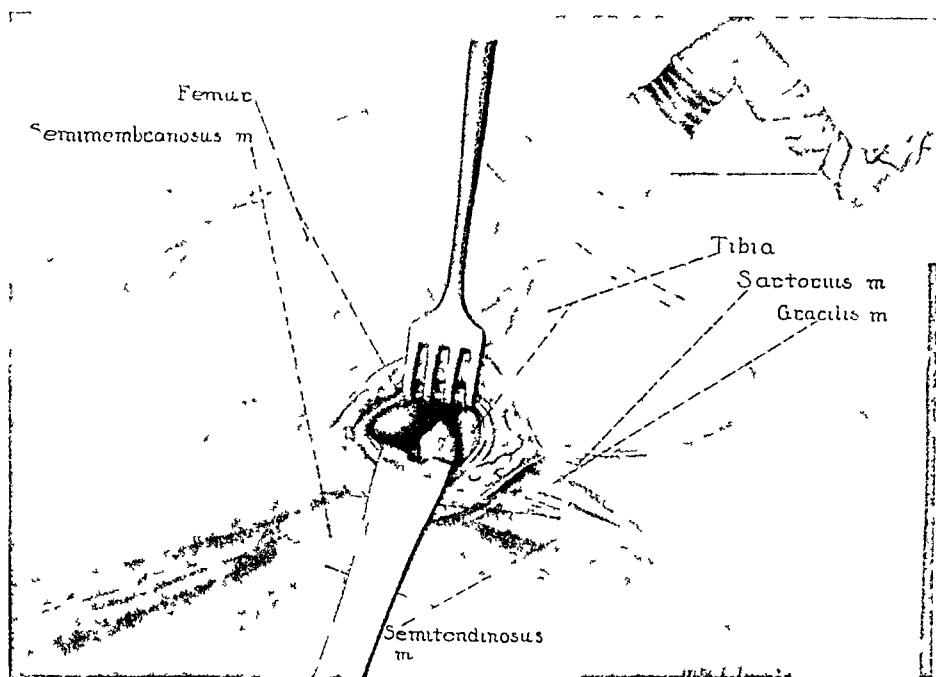


FIG. 6. Postero-internal incision for removal of loose bodies from posterior compartment. (From Henderson, in *Surg., Gynec. & Obst.*, 33: 698, 1921.)

varies greatly in cases of osteochondromatosis. Several cases have been reported in which more than a thousand loose bodies have been removed and there are many in which a hundred or more have been found in one knee joint.

Some recommend that a complete synovectomy be performed in every case, but in most of ours we have merely removed the wandering loose bodies and the bodies attached by pedicles. There have been few recurrences.

**Osteocartilaginous Bodies Due to Osteoarthritis.** Osteoarthritis of the knee is a common condition in elderly people. Not infrequently the osteophytic growths become very large and pieces break off within the joint and become wandering loose bodies. The number of these bodies rarely exceeds three or four. Many elderly patients have very little trouble with them and in that case removal is not advisable. However, if the bodies cause locking, they can be removed easily under local anesthesia. The patient must be warned that removal of the bodies will prevent the

and shape. Those which stay at the periphery of the joint and do not wander much are mulberry-like and rough, whereas those which are free to wander become very smooth and polished.

Sometimes the loose bodies retreat into the posterior internal or posterior external compartment where they cannot cause locking. In this situation they are best reached by posterior internal or posterior external incisions at the margin of the joint, just anterior to either hamstring. (Fig. 6.) With the knee partially flexed to relax the hamstrings, the capsule lies just beneath the skin and fat in this region. There is a median raphe in the midline and an instrument cannot be passed from the external posterior compartment to the internal or vice versa. If bodies lie in both compartments, bilateral incisions must be made.

#### RECURRENT DISLOCATIONS OF THE PATELLA

Recurrent dislocations of the patella are comparatively rare. In 1933,<sup>1</sup> I made a

study of a group of such cases at The Mayo Clinic and found that we had operated on thirty-five patients who had recurrent dislocations of the patella.

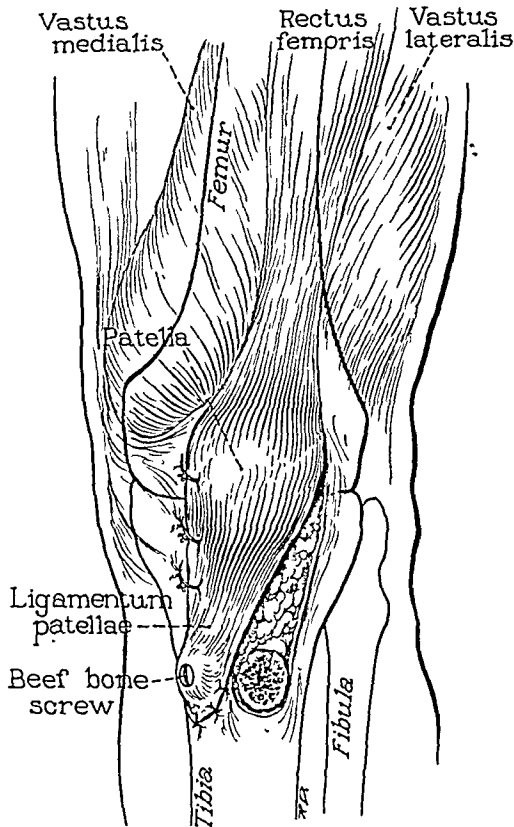


FIG. 7. Transference of insertion of ligamentum patellae inward to prevent recurrent dislocations of the patella.

The diagnosis is not always easy, for the surgeon seldom sees the patient when the patella is dislocated. The patient describes a sudden "giving-away" of the knee, accompanied by pain which is so severe that the abnormal position of the patella is not noticed. Usually some friend pulls on the knee and the patella "goes back" with a snap, much as happens when a semilunar cartilage is at fault. Since injuries of the cartilages are more common than dislocation of the patella, it is generally assumed that derangement of a cartilage has occurred.

There are several points in the differential diagnosis that are worthwhile. First, dislocation of the patella usually occurs in young women, whereas cartilaginous injuries usually affect men, predominantly; second, there is occasionally a family

history of dislocation of the patella, and third, the condition may have occurred previously in the opposite knee. It is better not to operate until there has been a suffi-

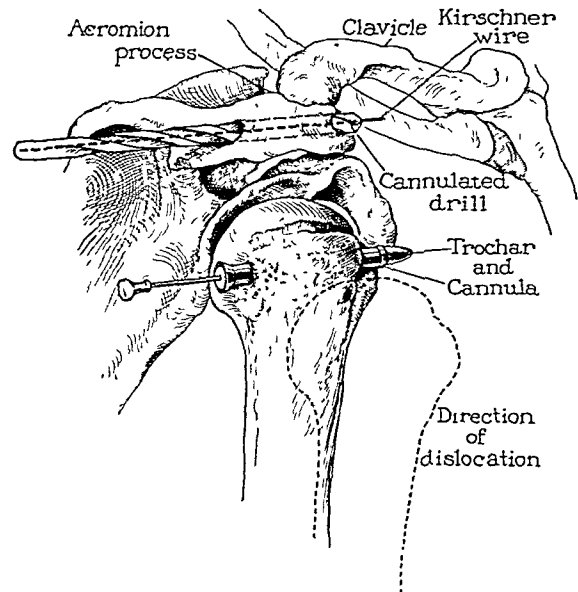


FIG. 8. Tenosuspension operation for recurrent dislocation of the shoulder. Diagrammatic drawing showing the method of drilling holes through the bone and the use of a trocar and cannula to facilitate insertion of the tendon. (From Henderson, in *J. Bone & Joint Surg.*, 33: 978, 1935.)

cient number of dislocations to enable the patient to tell whether the patella slips outward during the attack. A knock-knee deformity may be present. A clue may be obtained by the examiner in the following manner: He should sit beside the patient, see that the patient is thoroughly relaxed, the examiner holding the knee extended; then the examiner should gradually flex the patient's knee, at the same time pushing the patella laterally. As a flexion of about 150 degrees is reached the patient will usually grab for the knee and exclaim: "That is the way it happens."

The etiology is not certain. Some surgeons maintain that the external condyle is deficient, that is, the anteroposterior diameter is subnormal and thus the patella slips off it easily. Another explanation is that the patella is small and triangular in shape. Probably both of these contribute partially in causing the condition.

Swelling follows the attack and there may be ecchymosis, particularly at the

time of the initial dislocation. Ecchymosis is not commonly associated with derangements of the semilunar cartilages.

the patient will have considerable difficulty in flexing the knee, because the new contact areas of the patella and femur must be

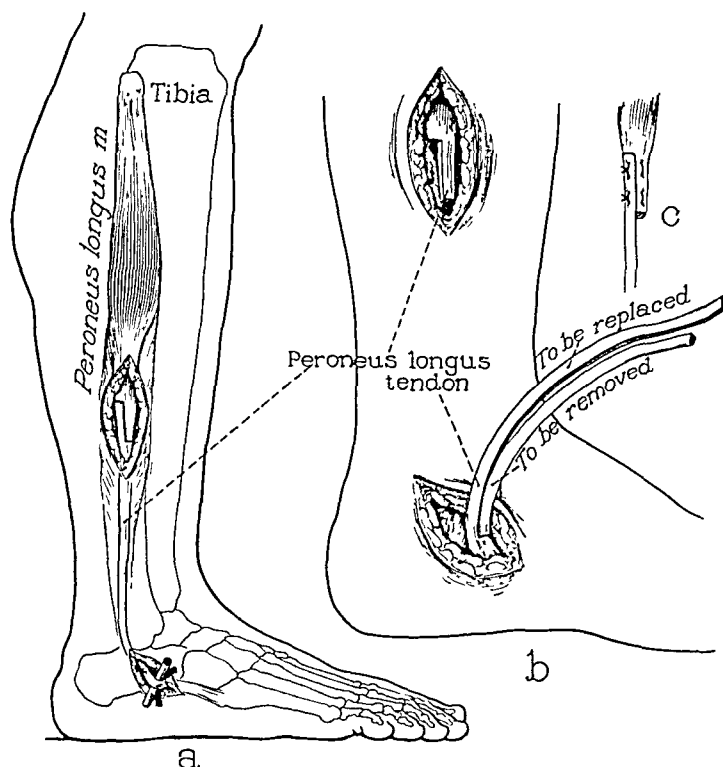


FIG. 9. Method of removal of a strip half the thickness of the peroneus longus tendon; the remaining half is sutured back into place. (From Henderson, in *J. Bone & Joint Surg.*, 33: 978, 1935.)

The treatment is simple in principle.<sup>1</sup> The operation which we prefer is one in which the insertion of the quadriceps tendon, along with a piece of bone of fair size is lifted up and transferred well inward and downward onto the flat internal surface of the tibia, so that when extension of the knee is attempted the pull of the quadriceps tendon will be such that the patella is pulled inward rather than outward. (Fig. 7.) If this procedure is carried out properly, the chances of failure are practically nonexistent. I believe that all the failures that we have had after this type of operation have been due to permitting too early use of the knee or to technical errors.

In our aforementioned group, there were thirty-nine operations on thirty-five patients, some of these patients requiring bilateral operations. In thirty-three of the cases, 94 per cent, the results were excellent. For about a year after the operation,

broken in, as it were. It is essential that the knee not be flexed sufficiently to exert a pull on the new insertion of the quadriceps tendon until this insertion has become firmly adherent in its new position, certainly not before three months have elapsed. When the quadriceps tendon and its insertion are transplanted, a large piece of bone should be taken up with it and then either placed in a carefully prepared slot in the cortex on the inner side of the tibia or held firmly to the bone by a beef bone screw or some such means until union develops.

#### OSTEOCARILAGINOUS LOOSE BODIES IN THE SHOULDER JOINT

Occasionally, loose bodies are to be found in the shoulder joint. They cause irregular painful catching and locking. It is our opinion that the loose bodies encountered in our cases were due to osteochondromatosis. Their removal relieved the patients.

Sometimes removal can be accomplished by a single posterior incision, since the capsule is more readily accessible at that point, and by manipulation of the shoulder and pressure on the joint bimanually, the loose bodies can be forced to the posterior compartment and removed.

#### HABITUAL OR RECURRENT DISLOCATIONS OF THE SHOULDER

This condition is commonly encountered among men, particularly those who engage in athletics. The etiology is not known, and considering the skeletal structure of the shoulder joint, it is a marvel that these habitual dislocations are not more common than they are. The head of the bone is held in place chiefly by muscular action.

Recurrent dislocations usually follow a primary traumatic dislocation. However, sometimes the initial dislocation follows such a slight strain that it cannot be called a true traumatic dislocation. Thereafter, dislocations occur on some trivial movement, such as stretching forward to grasp an object or even during sleep. Some authorities claim that the head of the humerus is misshapen, but in our cases we could not feel certain that this was true. In those cases in which the head was misshapen there had been so many dislocations and so many reductions that the distortion could be attributed to them. The patient is not only incapacitated and subject to much pain by the actual dislocations, but also becomes continually apprehensive and fearful of possible dislocation.

There are a number of surgical procedures available, and perhaps I can best illustrate the point that I wish to make by reviewing briefly the last report that I made on this condition in 1935.<sup>2</sup> Up to that time we had operated on sixty patients. In nineteen we had done the old capsulorrhaphy operation, i.e., reefing and overlapping the capsule as one would overlap tissues in an operation for hernia. The results in these cases were disappointing.

Only 37.5 per cent of the patients were completely relieved. We then turned to the Claremont operation, which consists of making a long posterior incision and lifting up the posterior fourth of the deltoid muscle, carrying it forward through the quadrilateral space anteriorly and then, by means of a small anterior incision, fastening it to the coracoid process. But again, the results were disappointing. Of eight patients, four, or 50 per cent, experienced a recurrence. Finally, in 1924, we turned to what I called the tenosuspension operation (Fig. 8), which consists of taking a piece of the peroneus longus tendon from the patient's leg and placing it through a hole bored in the head of the humerus and through a hole bored in the acromion process, thus making a suspensory ligament entirely extra-articular for the head of the humerus. This procedure has given us our best results. Of twenty-nine cases there were twenty-six, 90 per cent, in which further trouble did not occur, and the results in our later cases as we grew more experienced in the operation, have continued to be even better than that. The Nicola operation is the same as the tenosuspension operation in principle, but has the disadvantage that the tendon traverses the joint. This necessitates opening the joint and entails considerable dissection.

The postoperative period of disability in the tenosuspension operation is brief. The patient is usually in the hospital for only about ten days or two weeks. We now use only one-half of the peroneus longus tendon (Fig. 9) and the patient walks on the foot in a week without difficulty. We have had a number of athletes, such as boxers and swimmers, who have carried on very efficiently after the operation.

#### REFERENCES

1. HENDERSON, M. S. Derangements of the knee joint. *South. Surgeon*, 3: 123, 1934.
2. HENDERSON, M. S. Results following tenosuspension operations for habitual dislocation of the shoulder. *J. Bone & Joint Surg.*, 17: 978, 1935.
3. MORISON, RUTHERFORD. Injuries to the semilunar cartilages of the knee-joint. *Clin. J.*, 42: 1, 1913.

# THE INDUSTRIAL BACK FROM THE INTERNIST'S VIEWPOINT\*

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IN complete disregard of the multiple causes of backache, the tendency in industrial medicine is to "mass group" all these cases under the diagnosis of "back sprain." This error seems to be predicated upon the "locale" of the onset of pain. If it occurs while a man is cutting his own lawn, the term lumbago is invariably applied and the condition is attributed to causes within the man. However, if the pain arises while a man is stooping, bending or lifting at an industrial plant it is called back sprain and considered the result of motion while working for someone else. The situation assumes added import when it is appreciated that this disability is becoming one of the most frequent claims for compensation.

In the series offered for consideration, an *inadequate* or negligible history of injury occurred in over 70 per cent of the cases. Obviously, then, the history should determine the basis for investigation before accepting or denying the occupational origin. The patient brought in disabled because of a fall from a ladder or platform requires such an examination as will determine the extent of his injury, but the man who becomes disabled while engaged in a simple motion requires an investigation upon more divergent lines. It is imperative that criteria of normal and abnormal motion or movement be established in the examiner's mind. If the origin of pain is to be evaluated and its responsibility allocated, the above statement must become indelibly fixed in the minds of all industrial physicians.

Despite the contention that in the evolution of man instability of the lower back

occurred when he assumed the orthograde position, there does exist a normal, physiologic range of motion. Sprain is defined as an overstrain, the result of excessive motion. Accepting the last two statements as a premise, how can a motion to which one is accustomed, one executed daily in the same manner, one within the normal range and lacking the qualities of excessive, strenuous or unusual, constitute a sprain? Yet, beyond any question of doubt, mild to severe disabling pain does occur following a normal motion or a trivial act. Why? It should be apparent that it would not have occurred had there not been an added factor, an unrealized factor, present. It must be this added factor, this added "straw" that "breaks" the patient's back. The failure to search for it in industrial medicine has resulted in the preponderant diagnosis of back sprain.

The sacroiliac cause or theory will receive no mention other than to state that despite its refutation by reputable investigators it still finds wide acceptance. Invariably the diagnosis is made without benefit of x-ray. Such acumen is uncanny or simple sorcery. Sacralization, failure of fusion, abnormal articular facets, spondylolisthesis, horizontal sacrum, the narrowed intervertebral disc, herniation of the disc, hypertrophy of the ligamentum flavum, and contracture of the iliotibial band have been accepted or condemned as a cause of back pain. Judovich and Bates detract importance from the lumbosacral area and indict the dorsolumbar junction. Markoff attributes much back pain to a vasospastic disorder. Ridlon and Berkeiser call attention to the calcareous

\* From the Special Examination Department, Golden State Hospital (C. E. Early, M.D. and Associated Staff).  
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degeneration of the abdominal aorta as pertinent to backache. The author had one such unquestionable case in this series and eight others where this apparent circulatory deficiency was considered contributory. Gratz, using pneumofasciograms, demonstrates adhesions which he believes are the preponderant cause of back pain. Faulty posture, poor nutrition, insufficient exercise and ignorance as to how to execute motion are definite sources of back pain. Allergy, endocrine imbalance and referred pain from adjacent organs must be considered in this passing parade of possibilities. Finally, but most important, are the secondary effects from systemic or focal infection. Why this last mentioned source is accorded such negligible recognition by the industrial physician is beyond understanding. Pain occurring in the knee, elbow or shoulder invariably institutes a search for infection elsewhere in the body. Are the fascial planes and the vertebral joints not just as susceptible?

Consideration of all this varied etiology outlined in the review just completed stimulated the study offered in this paper and initiated three years ago. That the term *back sprain* could be applied to approximately 80 per cent of these disabilities appeared unreasonable and unscientific. It was felt that an adequate answer could be obtained only by studying a sufficiently large series of cases and only those cases where the onset of pain allegedly occurred while the patient was working. The series represents all ages, races, various social levels and all types of industry.

In the clinic where this material was gathered the following procedure is observed. Excluding the recently traumatized back (severe falls, crushes and blows) every patient alleging back pain is referred to the Special Examination Department. Following a detailed, exacting history and a complete physical examination, x-rays, urinalyses and blood counts are done routinely. If indicated and when necessary to establish the diagnosis, further x-rays of teeth, sinuses, lungs, genitourinary

tract, etc., are made; also blood Wassermann, blood chemistry, blood sedimentation, smears and cultures are taken. The data gathered from this three year study are presented in the tables.

TABLE I

(April 1, 1936–February 28, 1939)

No. of cases.....	3,018
Percentage of total clinic admissions, 1936.....	7.6
Percentage of total clinic admissions, 1938.....	10.4*
Males.....	2,799
Females.....	219
Average age.....	36.2 years
Patients referred to clinic diagnosed as back sprain.....	74 per cent
Patients referred to clinic diagnosed as sacroiliac disease.....	5 per cent
* Note the increase of 2.8 per cent of back claims in 1938 over 1936.	

Special attention is directed to the group of patients seen, treated, and diagnosed elsewhere before being referred to this clinic. These figures indicate that practically 80 per cent of the patients coming in from general industrial practice had been accepted as arising out of and due to occupation.

TABLE II

	No. of Cases	Accepted	Rejected	Percentage of Rejections
1936 (nine months)....	722	433	289	40
1937.....	1,092	564	528	49
1938.....	1,014	315	699	59
1939 (two months)....	190	56	134	71
Totals..	3,018	1,368	1,650	Average 57

The reason for the sharp rise in the percentage of rejections found in Table II is that in the summer of 1937 a policy of unlimited laboratory investigation was adopted. This resulted in finding pathology which, when considered with a negligible history of injury, formed a basis of rejection. While the entire average rejection over a three year period has been only 57 per cent, the rejections for 1938 and to date in 1939 averaged 70 per cent.

TABLE III

Findings	No.	Per Cent
Accepted cases. Contusion	423	31
Accepted cases. Leucocytosis		3
Rejected cases. Leucocytosis		37
Rejected cases. Abnormal urine, smears, serology, blood chemistry, etc		13
Rejected cases. History of previous back disability		42
Rejected cases. Fever		11

TABLE IV

Throat infection	301
Defective oral hygiene of significant degree	696
Coryza	127
Pleurisy	31
Pneumonia—pain in dorsal area first symptom	2
Cholecystitis	5
Gallstones	3
Aneurysm	1
Aortitis with positive serology	6
Coronary heart disease—suspected	12
Appendicitis, with chief complaint of back pain	3
Kidney stones	16
Nephritis with urinary evidence	63
Pyelitis	3
Cystitis	1
Hydronephrosis	7
Pyonephrosis	1
Acute gonorrhea (back pain reason for examination)	42
History of gonorrhea	512
Enlarged uterus—tumor	2
Abortion (called industrial doctor because of backache)	1
Abnormal prostate	208
Pylonic cyst (alleging its presence as resulting from contusion or strain)	26
Pernicious anemia (presented himself because of "sciatica" of legs from heavy lifting)	1
Tabes	3
Lead poisoning (back pain first symptom)	1
Bronchiogenic carcinoma (presented himself because of dorsal pain)	1
Cancer of prostate	3
Obesity (marked, with recurrent back pain but normal spine)	4
Obesity (marked, with recurrent back pain, with congenital defective spine)	9
Adiposogenital dystrophy (age 13; back pain after one day of lifting grocery baskets)	1

Tables III and IV comprise exhibit A in the indictment of the universal usage of the term "back strain" as a diagnosis of backache in the working man. Of the accepted cases, one-third revealed a history of actual contusion, leaving only two-thirds, or 945 out of 3,018 cases, to be accounted for by unusual stress or strain

or extraordinary circumstances. One cannot pass over lightly the fact that of the rejected cases 51 per cent had abnormal laboratory findings. Nor can one observe the extensive pathology listed in Table IV without realizing that the workman is subjected to the same ills all man is heir to and, therefore, the origin of his pain should not be stereotyped.

TABLE V

Patients x-rayed	2,414
Lumbosacral pictures	1,929
Cervical pictures	305
Dorsal pictures	180
Osteoarthritis	24 6 per cent
Cancer of vertebral bodies	6
Myeloma with involvement of spine	1
Kummell's disease	5
Nuclear expansions (Schmorl's cartilaginous nodules)	32 per cent

TABLE VI

Variations in lumbosacral area	1,929
Sacralization	14 6 per cent
Bilateral	5 2 per cent
Unilateral	9 4 per cent
Failure of fusion	18 4 per cent
Horizontal sacrum	3 4 per cent
Narrowed lumbosacral disc	52 per cent
Spondylolisthesis	2 8 per cent
Posterior displacement of fifth lumbar	21
Articular facet variations (incompletely studied)	1 6 per cent
Nucleus pulposus—herniation into canal	3

A narrowed lumbosacral disc found in 52 per cent of the cases is evidently a smaller number than that found by Williams and others. Our figure represents cases which showed not only a wedging of this disc but a diminution of the foramina. Efforts to determine cord pressure or blockage by posterior displacement of the nucleus pulposus have been but recently begun in the clinic so that we have no knowledge as to how often it might have been present in this series. Posterior displacement of the fifth lumbar is found in twenty-one cases in our series. We believe that these are not optical illusions, as Willis warns they are apt to be.

#### CONCLUSION

Any conclusion that backache has a multiple and varied etiology is redundant. There prevails no paucity of possible

causes. But the amazing revelation to be garnered from this study is that in spite of the recognized causes and irrespective of the possible pathology existing to explain backache, a diagnosis of assumption—a blanket diagnosis—occurs in 80 per cent of these cases. This paper contends that if a cause is sought by individual study of the case, a reversal of these figures takes place. This three year study would show that in the general industrial practice 75 per cent to 80 per cent of all back cases are considered occupational in origin and cited for compensation, whereas our clinic accepts only 30 per cent as arising from employment; and 70 per cent are denied compensation. The basis for this difference is to be found in personal opinion, interpretation of certain definitions, and in the employment of a thorough investigation.

1. The preformed mental attitude of the examiner. Prejudice, grievance or mercenary desire may automatically disfavor the employer or carrier; or the physician may favor the carrier too frequently by suspecting the majority of such patients as being malingerers. Personally, we believe that few, if any, acute back cases are true malingerers.

2. The individual interpretations of certain fundamental definitions.

- (a) Sprain. This has already been defined. To use this diagnosis, the examiner must weigh the alternates of usual or unusual, normal or excessive, an ordinary or an overt act.

- (b) The purpose behind and the philosophy of workman's compensation. Liability as intended by this code must be squarely interpreted. Liability can be imposed for only those disabilities that are caused or aggravated by circumstances, conditions and environment which constitute a hazard and to which normally one would not be subjected. Therefore, one must ask, does normal motion constitute an industrial hazard?

Finally, from the internist's viewpoint, the disabling back is not an industrial entity. The practice of according it the same occupational earmarks as are attri-

buted to silicosis or lead poisoning, for instance, is a fallacy. Such an assumption constitutes an economic injustice to industry in general as well as an unjust consideration of the patient who deserves a diagnosis. From the internist's viewpoint the so-called "industrial back" is not primarily an orthopedic problem. It is one for differential diagnosis. From his viewpoint and study, disease and infection comprise a considerable portion of the etiology.

#### REFERENCES

1. GOODWYN, T. P. Effect of trauma on mechanically weak back. *Am. J. Surg.*, 42: 577, 1938.
2. HODGES, F. J., and PECK, W. S. Clinical and roentgenological study of low back pain with sciatic radiation; roentgenological aspects. *Am. J. Roentgenol.*, 37: 461, 1937.
3. WILLIAMS, P. C. Lesions of lumbosacral spine; acute traumatic destruction of lumbosacral intervertebral disc. *J. Bone & Joint Surg.*, 19: 343, 1937.
4. PUTTI, V. New conceptions in pathology of sciatic pain. *Lancet.*, 2: 53, 1927.
5. OBER, F. R. Role of iliotibial band and fascia lata as factor in causation of low back disabilities and sciatica. *J. Bone & Joint Surg.*, 18: 105, 1936.
6. GRATZ, C. M. Fascial adhesions in pain low in back and arthritis. *J. A. M. A.*, 111: 1813, 1938.
7. WILLUS, THEO. Low back pain. *J. Bone & Joint Surg.*, 15: 745, 1934.
8. NAFFZIGER, H. C. Neurological aspects of injuries to spine. *J. Bone & Joint Surg.*, 20: 444, 1938.
9. MOFFAT, B. W. Enlargement of intervertebral disc associated with decalcification of vertebral body; compensatory hypertrophy. *J. Bone & Joint Surg.*, 15: 679, 1933.
10. STEINDLER, ARTHUR. Differential diagnosis of pain low in back; allocation of source of pain by procain hydrochloride method. *J. A. M. A.*, 110: 106, 1938.
11. BARR, J. S., HAMPTON, A. O., and MIXTER, W. J. Pain low in back and "sciatica" due to lesions of intervertebral discs. *J. A. M. A.*, 109: 1265, 1937.
12. SCHMITTER, F. Sciatica and fibrositis; historical and recent cults, theories and facts as to etiology, diagnosis, and treatment. *Indus. Med.*, 7: 82, 1938.
13. COLE, J. P. Low back conditions; diagnosis and treatment. *Indus. Med.*, 6: 609, 1937.
14. BAILEY, W. Anomalies and fractures of vertebral articular processes. *J. A. M. A.*, 108: 266, 1937.
15. SPURLING, R. G., MAYFIELD, F. H., and ROGERS, J. B. Hypertrophy of ligamenta flava as cause of low back pain. *J. A. M. A.*, 109: 928, 1937.
16. ABBOTT, W. D. Compression of cauda equina by ligamentum flavum. *J. A. M. A.*, 106: 2129, 1936.
17. GAENSLEN, F. J. Low back pain; etiology, diagnosis, and treatment. *Indus. Med.*, 4: 105, 1935.



# A RENAISSANCE OF SUTURE TECHNIQUE NEEDED

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A RECENT editorial in the *Journal of the American Medical Association*,<sup>1</sup> entitled, "The Renaissance of Silk in Surgery," must be viewed with considerable disquietude. Apparently a cycle of surgical technique has been completed, and we are now about to enter a new one making the same mistakes which we did not learn to avoid in the last. A general recommendation for silk cannot ignore the contraindications for the use of this material, nor can the surgical technique generally employed for suturing be transposed to the use of silk without causing a greater number of complications than is encountered at present. After Lister introduced "antiseptic" catgut, many surgeons continued to have wound complications as before, but at least, as Godlee pointed out, the introduction of the antiseptic absorbable suture retired to oblivion the use of non-absorbable sutures with ends hanging out of the wound in order that they might be removed later when suppuration started. Kocher with his "fort mit dem Catgut" successfully introduced the use of "antiseptic" silk on the continent, and his work inspired Halsted to use silk with equal success in this country.

But Halsted fully realized the danger of every surgeon's adopting the use of silk, and those who quote him usually fail to repeat what he said about a proper technique for this material.<sup>2</sup> His catgut-silk paradox is as follows:

"Paradox, because (1) a surgeon uses catgut because he cannot get good results with silk—has stitch abscesses continually from ligatures as well as sutures. (2) A good surgeon (Kocher for example) says, 'I have no trouble since I gave up catgut and commenced using silk exclusively.' The surgeon hears this and says, 'Well, now I understand why so few of my wounds heal well. I should have used silk in-

stead of catgut.' I said, 'Don't try silk, you will have more trouble than with catgut.' Explanations followed. A bad technique will get best results with catgut. A good technique best results without catgut, that is silk. Good and bad results are relative terms. Almost anyone can get pretty good results with catgut but no one gets perfect results with catgut. To prevent even an occasional failure the good technician resorts to silk. In the hand of a bad technician silk is disastrous."

Silk found wide acceptance in Europe on the recommendation of Kocher, but soon chronically draining sinuses began to result from operative wounds which became infected and these were finally so prevalent that surgeons working in the out-patient departments carried crochet hooks as standard equipment to "fish out" silk sutures. More recently, Whipple<sup>3</sup> has told of the necessity of abandoning the use of silk when he first introduced it on his service because of lack of proper employment and the complications which developed. Shambaugh<sup>4</sup> has also indicated that the use of silk was abandoned for a number of years at the Peter Bent Brigham Hospital. The use of silk will also suffer setbacks in this renaissance if the warnings regarding its mode of employment are not carefully heeded. The crochet hook should not return again, but already commercial houses are selling silk "for use in general surgery" of diameters two or three times the correct sizes recommended by Halsted.<sup>5</sup>

Certainly there is no need to use silk because of catgut allergy, and more important still, the use of catgut should not be given up for this reason. The myth of catgut allergy needs to be exploded once and for all. Is it not unusual if there is a true allergy for catgut, that the only manifestation of this allergy is an inflammatory reaction in the wound which can also be

produced by tying sutures too tightly or from not observing a rigid aseptic technique? In the single instance reported in the literature of a supposed allergic manifestation to catgut other than a complication of wound healing, Tripp<sup>6</sup> theorized that his female patient developed asthma after an operation because her incision had been sutured with catgut, but he did absolutely nothing to prove that the attack had not resulted from one of many other causes of asthma.

Moreover, when experiments are quoted in support of the thesis of catgut allergy, apparently the investigations of Reil,<sup>7</sup> Frugoni,<sup>8</sup> and Gratia and Gilson<sup>9</sup> are forgotten because they do not indicate that a specific allergy exists. These workers demonstrated, for example, that (1) catgut cannot be antigenic as it is absorbed and, therefore, could not produce an acquired hypersensitive state; (2) precipitation tests for catgut antibodies were negative, showing that a natural hypersensitive state does not exist; and (3) any reaction produced with catgut after so-called sensitization is nonspecific.

Recently, from the Royal University of Pavia, Beluffi<sup>10</sup> reported the results of an extensive investigation on the subject of catgut allergy, and came to the conclusion that "catgut does not possess antigenic properties; the previous introduction and absorption of catgut do not produce a sensitization toward it or toward other proteins; and the reactions to catgut are interpreted not as allergic phenomena but more probably as foreign body reactions." Finally, just a few months before this editorial<sup>1</sup> appeared, Pickrell<sup>11</sup> was unable to substantiate the work of Kraissl<sup>12,13</sup> which was quoted in the editorial as the proof of catgut allergy. In this investigation at Johns Hopkins University, no wound disruption occurred in either rabbits or guinea pigs previously treated with catgut when proper aseptic precautions were observed in the repair of the wound. Pickrell pointed out that, in Kraissl's illustrations, one of the wounds

which disrupted shortly after the repair occurred on an abdominal wall inadequately shaved. Besides, neither guinea pigs nor rabbits, as Kraissl had claimed, could be sensitized to commercial catgut, or to a catgut extract furnished by Kraissl, and no evidence of sensitivity to catgut could be demonstrated in three patients whose wounds disrupted. In this regard, it should be mentioned that Glenn and Moore<sup>14</sup> found an incidence of disruption of 0.68 per cent in catgut sutured wounds and 0.61 per cent when silk was used. Lastly, in one hundred patients tested with catgut extract before and after operation, no sensitivity could be demonstrated; and therefore Pickrell concluded "that although catgut, like any other suture material, acts as a foreign body and causes a slight leukocytic response, it does not act as an antigen to induce the hypersensitive state." The truth, then, should be admitted that a poor suture technique undoubtedly accounts for the wound healing complications too glibly attributed to catgut allergy.

It can reasonably be questioned how much the comparison of the results of the healing of clean wounds sutured with silk and catgut is influenced by better suture technique and the use of fine sizes when silk is employed. Indeed, the most rabid proponent of silk would admit that catgut is the better suture material if large sizes of silk were used by the technique of suturing usually employed for catgut.

Too often the indications and contraindications for the different suture materials are forgotten. The best example of this comes in the form of a letter written to the *Journal of the American Medical Association*<sup>15</sup> praising this same editorial and stating that ever since catgut and clips had been abandoned in mastoid operations (for what other reason than to close the skin?) the results have been excellent. Elementary as the statement must seem, to some, apparently, it must be reiterated again and again that catgut cannot be used to suture the skin because suppuration and

complications invariably develop. In other words, the use of catgut in the skin is definitely contraindicated. Equally as obvious, but apparently as frequently overlooked, is the fact that catgut should not be used in the subcutaneous fat except as very fine interrupted sutures to repair a subcutaneous fascia if this layer is sufficiently well-developed; better still, that catgut should not be used at all in this location. Induration of the wound results and, as Halsted pointed out, a few drops of serum are discharged on the ninth or tenth day. Silk also has its contraindications. It cannot be used with any degree of safety to suture the mucosa of hollow viscera. Mitchell<sup>16</sup> and Soresi<sup>17</sup> have reported the formation of chronic ulcerations about silk sutures in the gastrointestinal mucosa, and in the mucosae of the urinary bladder and gallbladder nonabsorbable sutures act as *nidi for calculi*. On the other hand, there is no question about the efficacy of silk in thyroid surgery and for the repair of cut tendons and nerves.

When these indications and contraindications are considered, it is obvious that in the repair of clean wounds in different tissues the best results will not always be obtained by using one type of suture material; that both catgut and silk are needed and probably will be for some time. In spite of all that has been written against the absorbable suture for the repair of the clean wound, catgut is still used by the great majority of surgeons, although admittedly rather poorly, and the principle of absorbability of the suture has definite merit. Neither can the fact be ignored that catgut is almost universally used for the repair of contaminated wounds, although Shambaugh and Dunphy<sup>18</sup> write that wounds repaired with silk tolerate bacterial contamination better than similar wounds repaired with catgut. However, they used much larger catgut than silk, and the simple law for the comparison of the chemical nature of foreign bodies dictates that physically they should be of the same magnitude.

There is no doubt that the healing of wounds could be immensely benefited in general by improving suture technique, but the endless argument about the type of suture material to use totally obscures this solution. Suturing is still in the basting stage and the selection of the size required is judged more, as Harvey<sup>19</sup> points out, on the basis of the physique of the operator than on the needs of the tissue. "Anyone," says Dew,<sup>20</sup> "who has watched surgeons in many parts of the world carry out this simple procedure of closing the wound cannot help being struck not only by the diversity of the methods used, but even more by the variability of the healing process." And yet the principles involved are very definite. At the risk of being didactic instead of platitudinous, they are listed below along with specific recommendations.

1. Suture the cut edges to obtain healing in the shortest possible time after the infliction of the wound and not solely for the purpose of securing them as safely as possible.

2. To do this, sutures must not be made the agents for transplanting bacteria into the wound. The clean wound is never sterile. Sutures pick up bacteria (1) by being soaked in a basin previously used to wash instruments coming from the wound; (2) by coming in contact with exposed skin edges, and (3) from repeated handling. The ligature on the spool, for example, repeatedly comes in contact with the blood from the wound and with the hands of the operator, concentrating the bacteria on the unused portion of the suture. "Finger surgery" is an excellent method to move the bacteria about the wound. Ives and Hirschfeld<sup>21</sup> have shown that the majority of postoperative wound infections are caused by bacteria similar to those isolated from the wound at operation.

3. Sutures should not be inserted and tied in such a manner as to create necrotic tissue in which the bacteria may grow. The bite of tissue included in the suture should be small, about  $\frac{3}{8}$  of an inch when

tied, and tied loosely. The edema that develops in the wound during the first forty-eight hours tightens the sutures further. The tightness required for skin sutures should be used as the guide for the tightness of deep sutures. The redness and infection which develop around the skin suture tied too tightly indicate the effect of the same degree of strangulation on the more easily necrotized muscle and fat. Large tufts of tissues should not be tied off by ligatures. The tuft should not be visible. Excellent wound healing results when healthy cells are placed in contact with healthy cells. Because of the danger of necrosis resulting from tension on the sutures, layers of tissues which will not lie together should not be sutured together. Rather than attempt to approximate tissues under tension by means of sutures, one should release tissues by plastic incisions or not suture them at all. They usually separate again anyway.

4. Traumatic wounds seen eight hours or more after infliction should not be sutured because bacteria have already begun to multiply.

5. Sutures should be used sparingly. They are foreign bodies and, as such, aid in developing a bacterial infection. The common error is to use too much suture material and especially too large sizes. Because of the inability of the tissues to hold larger sutures, there is no need to use a suture larger than No. 0 catgut or its equivalent size of silk. Exceptionally, a larger strand may be needed to set the knot, but not to hold the tissues.

6. In order that sutures may be used sparingly and yet have the greatest mechanical advantages, interrupted sutures should be used with triple throw knots, all tied square. Taylor<sup>22</sup> has shown that such knots provide the greatest security. Tissues having the greatest holding power for the sutures or possessing a mechanical advantage should be sutured—the peritoneum, the fasciae, and the skin. The rest of the tissues do not need to be

sutured except under special circumstances. The suture should be of such a type that it pulls at right angles to the tissue fibers and not parallel to them.

7. The clean wound made to drain an infected focus, as for example an appendiceal abscess, should not be contaminated during operation. Laparotomy pads provide protection, and suction should be used to remove the pus. After the peritoneum is closed, the wound is treated as a traumatic wound, freshly contaminated, namely, by irrigation and debridement. Subsequent drainage seeps less between the layers if the drains are placed at one end of the wound. There is no need of the defeatist attitude that all such wounds become infected, and that therefore the layers above the peritoneum should be left open to heal by secondary intention.

8. The skin edges should be everted by the sutures.

9. Attention to details and meticulous care in handling the tissues, instead of haste, cannot be overemphasized. The surgeon may save five or ten minutes in closing the wound rapidly, whereas the patient may lose several weeks and his life may be endangered, fighting an infection.

#### REFERENCES

1. Editorial. Renaissance of silk in surgery. *J. A. M. A.*, 113: 1417, 1939.
2. MACCALLUM, G. William Halsted—A Biography. Baltimore, 1930. John Hopkins Press.
3. WHIPPLE, A. O. Address, before American College of Surgeons. Philadelphia, October, 1939.
4. SHAMBAUGH, P. Postoperative wound complications. A clinical study in reference to silk. *Surg., Gynec. & Obst.*, 64: 765, 1937.
5. HALSTED, W. S. Ligature and suture material, etc. *J. A. M. A.*, 60: 1119, 1913.
6. TRIPP, H. D. Catgut allergy. *J. Indiana State M. A.*, 28: 383, 1934.
7. REIL, H. Beitrag zum Catgut Problem. *Chirurg*, 4: 27, 1932.
8. FRUGONI, P. Sulla supposita allergia da Catgut, ricerche sperimentali. *Arch. ital. di chir.*, 42: 334, 1936.
9. GRATIA, A., and GILSON, O. Le phénomène d'Arthus au catgut cause insoupçonnée d'accidents post-opératoires. *Bull. Acad. de méd. de Belgique*, 14: 125, 1934.
10. BELUFFI, E. L. Ricerche sperimentali sull'allergia da catgut. *Clinica Chirurgica*, 15: 109, 1939.

11. PICKRELL, K. L. Studies on hypersensitivity to catgut as a factor in wound disruption. *Bull. Johns Hopkins Hosp.*, 64: 195, 1939.
12. KRAISSL, C. T. Intrinsic factors alternating the absorption of catgut. *Surg., Gynec. & Obst.*, 63: 561, 1936.
13. KRAISSL, C. T., KESTEN, B. M., and CIMIOTTI, J. G. The relation of catgut sensitivity to wound healing. *Surg., Gynec. & Obs.*, 66: 628, 1938.
14. GLENN, F., and MOORE, S. W. The disruption of abdominal wounds. *Surg., Gynec. & Obst.*, 65: 16, 1937.
15. PHILLIP, FRANK. Correspondence. *J. A. M. A.*, 113: 1829, 1939.
16. MITCHELL, A. B. Gastric and duodenal ulcers. A record of 110 recent operations. *Ann. Surg.*, 54: 806, 1911.
17. SORESI, A. L. Secondary ulcers of stomach and jejunum. Formation of calculi around unabsorbable material used in suturing intestinal mucosa. *Ann. Surg.*, 61: 328, 1915.
18. SHAMBAUGH, P., and DUNPHY, J. E. Postoperative wound infections, and the use of silk: an experimental study. *Surgery*, 1: 379, 1937.
19. HARVEY, S. C. Concerning the suture. *Surg., Gynec. & Obst.*, 58: 791, 1934.
20. DEW, H. The closure of surgical wounds. *Australian & New Zealand J. Surg.*, 8: 315, 1939.
21. IVES, H. R., JR., and HIRSCHFELD, J. W. The bacterial flora of clean surgical wounds. *Ann. Surg.*, 107: 607, 1938.
22. TAYLOR, F. W. Surgical knots and sutures. *Surgery*, 5: 498, 1939.



By the term sprain is meant an injury which involves minute traumatism only, as the rupture of individual fibers. By the term torn ligaments is meant a more severe injury with abnormal mobility of the joint.

# ACUTE MASTITIS

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THE breasts are subject to the same inflammatory vicissitudes that affect other parenchymatous organs. No age is exempt and both sexes may be affected. It is true that the invading pyogenic organisms prefer the lactating gland but not infrequently they find a suitable haven in the non-functioning breast. For instance, we have obtained cultures of *Staphylococcus aureus* from the discharging nipples of infants. Such a neonatal mastitis represents a suppurative reaction superimposed on a physiologic hypertrophy of the breast tissue due to stimulation of the maternal endocrine glands. These infections are short lived, seldom form abscesses, and usually subside under conservative therapy.

Juvenile or prepubescent mastitis is usually preceded by trauma. Hematomas and devitalized tissues furnish a succulent nidus for wandering pathogens. Figure 1 is a photograph of an 8 year old girl who fell and injured her left breast while suffering from a sore throat. Two days later, the breast became swollen and tender, and the axillary glands were enlarged and "sore." No frank abscess formed but the secretions aspirated from the inflamed matrix contained a streptococcus having the same morphologic and cultural characteristics as those recovered from the throat. Occasionally a prepubertal mastitis may occur as a complication of mumps or as a sequel of an axillary abscess. (Fig. 2.)

*Lactation Mastitis.* It is common belief that lactation is the most important predisposing factor of acute mastitis.<sup>2</sup> If one considers cracked nipples, trauma, vascular engorgement and stasis of milk as part of the normal process of nursing, then this concept is true.

Much has been written about "caked breasts" and stagnation of milk as being the chief precursors of suppurative masti-

tis. Sherrick<sup>15</sup> believed retained breast secretions were chemically irritating to the parenchymatous tissues. Keynes<sup>11</sup> maintained such secretions acted as irritants only when reabsorbed. Klahn<sup>10</sup> found those women whose breasts were completely evacuated by means of a pump rather than by nursing did not develop a mastitis. He felt the mechanical evacuation eliminated both stagnation and trauma. Dippel and Johnston<sup>7</sup> pointed out that acute mastitis occurred most frequently during the first two weeks of lactation and it was during this period that stasis of milk and the incidence of "caked breasts" were the highest. It seemed to them the stagnant milk was an excellent pabulum for any lurking pathogens.

While the above arguments have much merit it seems to us they have received undue emphasis. DeLee<sup>6</sup> affirmed that the simple retention of milk seldom terminated in an inflammatory reaction. Williams<sup>16</sup> pointed out that if an artificial stasis of milk were produced by obstructing the orifices of the lactiferous ducts, a suppurative process developed only when pathogenic bacteria were introduced. Actual clinical studies have confirmed this observation.

Mrs. R., housewife, 26 years of age, was referred to the University Hospital with the diagnosis of a "caked breast" associated with a localized abscess. She had successfully nursed her 8 month old child until two days prior to admission, at which time she decided to wean him. In spite of the fact that she produced a copious supply of milk she refused to empty the breasts mechanically. Both mammary glands became engorged, tender and "hot." A milky discharge seeped from the nipples and for twelve hours she suffered excruciating pains. That she was extremely ill was evidenced by a temperature of 103.6°F. and a leucocytosis

of 23,000. It was apparent that the engorgement was due to the retention of breast secretions, but it was felt that the hyperthermia,



FIG. 1. Acute streptococcal juvenile mastitis due to injury of breast while suffering from tonsillitis.

the leucocytosis and the exquisite tenderness resulted from a secondary pyogenic infection. After evacuating the breasts with a pump, 15 c.c. of a contrast medium were introduced into one of the discharging estuaries and a simple roentgenogram taken. The ampulla and all of its communicating lacteals were found to be enormously distended but otherwise normal. (Fig. 3.) Cultures of the aspirated secretion were sterile. This mammographic study clearly demonstrated that the intense mastalgia, the turgidity of the breasts and the systemic reactions were all caused by a retention of normal breast secretions and not by a septic infection.

Mammographic visualizations have also demonstrated that the so-called "caked breast" is not due to an obstructive retention of secretions in the lactiferous tubules but rather to a congestion of the secreting cells themselves. Mammograms have re-

peatedly shown the ducts leading from "caked" lobules to be patent and on no occasion have secretions been recovered by aspirating the cannulated ducts. (Fig. 4.) The induration and swelling in a breast thus affected are due therefore to the vascular and lymphatic engorgement of the duct walls and to an edema of the epithelial cells which line the acini. These congested cells do not secrete milk. Interestingly enough, these "caked" lobules seldom suppurate unless trauma and infection are superimposed.

Most workers believe that the *Staphylococcus aureus* is usually the provocative agent in acute mastitis. Occasionally, however, the *Staphylococcus albus*, streptococci, colon bacilli and mixed infections are encountered. It requires more than the mere presence of bacteria to produce acute mastitis. It has long been known that bacteria may inhabit the lactiferous ducts of an apparently healthy breast. Moon and Gilbert<sup>13</sup> studied the milk of 100 normal lactating mothers and found that in 50 per cent of the cases pathogenic organisms could be recovered from the milk, and yet they did not develop an inflammatory reaction. Apparently the resistance of the local tissues must be reduced by such factors as trauma or stasis before the pathogens can gain a foothold.

The invading organisms gain entrance to the breast by one of four routes: ascension along the ducts, through the lymphatic system, through the blood stream, or by direct extension. Dawson<sup>5</sup> pointed out that in the non-functioning gland the orifices of the ducts are occluded with keratinized plugs of debris, but that with the advent of lactation the ducts become patent, thus affording an easy entrance for any pathogens lurking on the surface of the nipples or in the mouth of the suckling child. In some instances the bacteria which are already inhabiting the lacteals assume pathogenic powers. The high incidence of acute mastitis associated with cracked nipples strongly suggests that the organisms invade the parenchymatous tissues

through the lymphatic channels. Dippel and Johnston<sup>7</sup> firmly believe that acute infections of the mammary gland are much

the induration progresses to the stage of liquefaction and abscess formation.

It is most difficult to determine when an



FIG. 2. Acute mastitis of right breast caused by a retrograde lymphangitis associated with an axillary abscess.

more common after instrumental or surgical deliveries than after normal childbirth. They affirm that the bacteria are carried from the traumatized pelvic organs to the breast by the vascular route.

It is apparent that no one agent can be singled out as being the provocative factor in acute mastitis, but that it requires the combined forces of many. Any condition which reduces the resistance of the breast tissues and introduces virulent organisms may perpetrate a suppurative reaction.

#### SYMPTOMS

The symptoms of acute mastitis are rather definite and not difficult to recognize. At first the affected lobules become swollen, tense, and tender. The excruciating mastalgia makes nursing a painful ordeal and results in an incomplete emptying of the milk ducts. The skin assumes a dusky, brawny color and the resulting edema accentuates the pitting of the skin, making the little depressions seem more widely separated than normally. If the acute mastitis does not respond to conservative therapy within three or four days,



FIG. 3. A mammogram of an enormously dilated ampulla and its communicating radicle caused by retention of breast secretions.

inflammatory process has progressed to the state of abscess formation and yet such information is essential to correct therapy. Usually the acute mastitis becomes localized, the induration increases and the patient acquires a septic appearance. The subareolar and subcutaneous varieties soon point, and fluctuation can be easily demonstrated, but in the deep-seated intramammary and retromammary types the induration becomes so pronounced that it completely obscures all semblance of fluctuation and may be mistaken for a solid tumor. In rare instances, the abscess may communicate with the ducts and discharge its purulent contents from the nipple.

It is of vital importance that suppurative lesions should be differentiated from inflammatory carcinoma. Kilgore<sup>12</sup> found that 25 per cent of all cancers occurring in the lactating breast were discovered during the early months of lactation, many during the first four weeks. Under such circum-



stances, it was quite natural to assume that the malignant neoplasms were merely inflammatory processes rather than true

less susceptible to the trauma and maceration of frequent nursing.

It is during the period of engorgement

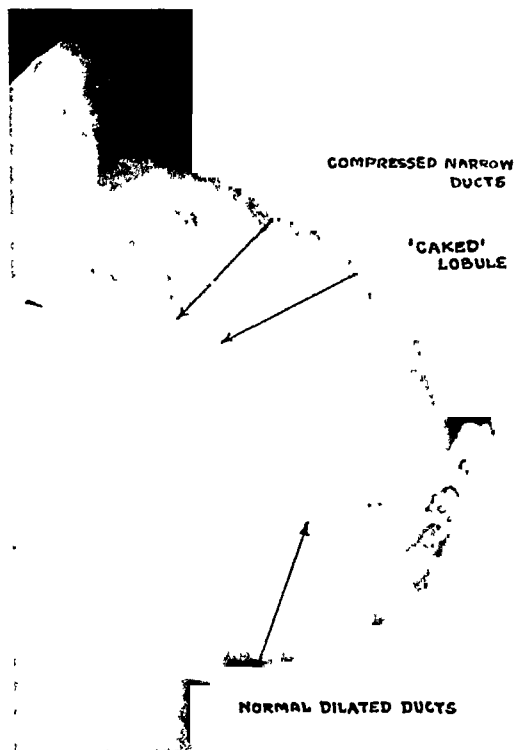


FIG. 4. Observe the large dilated ducts of normal breast lobule as compared to the compressed narrowed lumen of those of the "caked lobule." All ducts are patent.

cancers. In some instances, several months passed before a correct diagnosis was made, and by that time the carcinoma was so extensive that only palliation could be offered to the patient. Aspirational and exploratory biopsies may be necessary to make a correct diagnosis.

#### TREATMENT

*Prophylactic Therapy.* It is much easier to prevent abscesses from forming than it is to cure them. Particular attention should be paid to the nipple during the last two months of pregnancy in order to prepare it for the ordeal of nursing. A gentle stripping massage not only develops the fibrous and muscular structures, but it makes the nipples stand more erect, thus making nursing much easier. Daily inunctions with hardening solutions render them

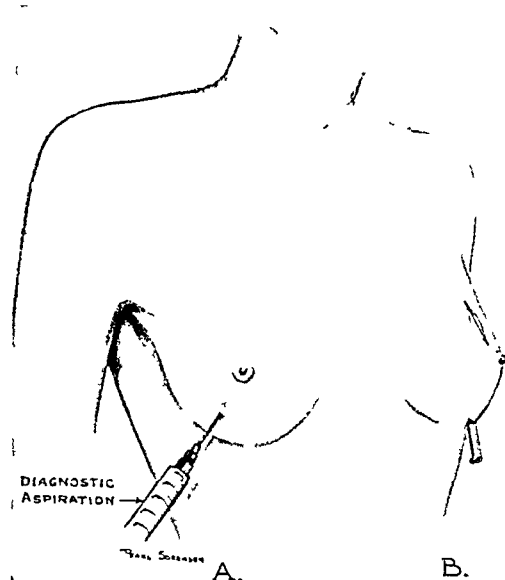


FIG. 5. A, diagnostic aspiration of an inflammatory mass to determine the presence of pus. B., establishing dependent drainage in an abscess which had "pointed" above the nipple.

that vigilance is of paramount importance. Cracked and fissured nipples require immediate attention, as painful nursing inevitably leads to incomplete evacuation of the breast with subsequent stagnation and possible infection. The use of hot boracic acid compresses, nipple shields, breast pumps, ultraviolet light and short wave diathermy will do much to expedite the healing of sore nipples. If the breast becomes "caked," the concern should not be for the affected lobule but for the unaffected segments. Seldom does the "caked" lobule suppurate, for it is a congestive and not an inflammatory process. It is dangerous only in that the associated mastalgia interferes with complete evacuation of the uninvolved lobules. If nursing becomes so painful that complete emptying is not obtained, then a breast pump should be employed. Massage, stripping the nipple, or too forceful attempts to evacuate the distended areas are detrimental. The resulting trauma accentuates the congestion, produces small regional hematomas which

furnish an inviting place for bacterial growth.

Even in the presence of acute inflamma-

Irradiation possesses definite curative properties in the early non-suppurative mastitis, if used correctly. Hunt<sup>9</sup> maintains

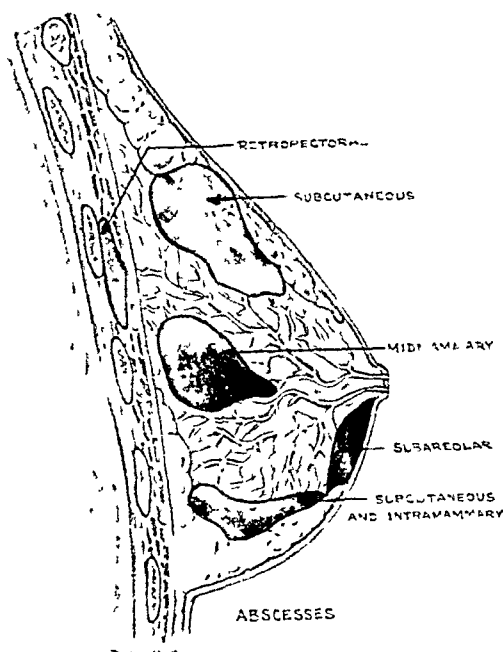


FIG. 6. Various types and locations of mammary abscesses

tory reactions, conservative therapy will bear fruit, for not every inflammatory mass requires surgical drainage. In fact, most of them can be aborted before they reach the point of suppuration. All nursing should be suspended as the resulting trauma aggravates the lesion and the ingestion of contaminated milk might prove harmful to the nursing. In mild infections the breast pump is effective in completely evacuating the ducts. If, however, the entire breast is involved, all attempts, both real and artificial, to empty the breast should be prohibited. Hot fomentations and cold packs have both proved effective, but the former seem to possess greater powers of analgesia. We have found that short wave diathermy, given four or five times a day, relieves the congestion and mitigates the discomfort. This dry heat not only prevents the maceration of the skin which may accompany the frequent use of moist compresses but it also deposits the heat within the deeper tissues where it is most effective.



FIG. 7. A persistent sinus and milk fistula caused by severing the milk ducts while draining an intramammary abscess.

that it not only arrests the progress of the infection but accelerates the resolution of the inflammatory mass.

#### MANAGEMENT OF THE BREAST ABSCESS

Frank suppuration calls for immediate drainage. Procrastination merely permits the infectious process to destroy adjacent tissues and convert a simple abscess into an extensive multilocular lesion. It may be extremely difficult to determine when an inflammatory tumor has undergone suppuration. It is common practice to wait until fluctuation can be demonstrated, or until the abscess points, before resorting to surgical interference. Such a practice is certainly not without danger, for in the presence of intramammary and retromammary abscesses, one is not always able to demonstrate fluctuation. Whenever there is doubt, the aspirating needle is enlightening. (Fig. 5A.) If pus is encountered, the abscess should be drained regardless of whether fluctuation can or cannot be demonstrated. There should be no hesi-

tancy in performing diagnostic aspirations, for a single puncture does not disseminate the infection and immediate drainage is much better than expectant treatment.

The surgical management cannot be standardized as it varies with the size, location and extent of the abscess and the functional status of the mammary gland. (Fig. 6.)

*Subareolar abscesses* are usually superficial and, as the infection follows along the larger ducts, it naturally points to the surface. Being small and involving only the subcutaneous tissues, these abscesses can be drained effectively by a small circumareolar incision. It should not extend below the dermis for fear of severing the large ductal ampullae which may result in an annoying milk fistula. (Fig. 7.) The abscess proper is opened by inserting a blunt forceps into the inflammatory mass. It is extremely important to determine whether the subareolar abscess communicates with a larger intramammary pocket of pus as the latter requires more radical drainage.

*Subcutaneous abscesses*, when they occur singly, are easily recognized and can be drained effectively by radial incisions. They offer no problem unless they are of the "dumb-bell" type with an underlying midmammary abscess.

*Intramammary abscesses* present a more complex problem. The suppurative process becomes rather extensive before it spreads to the overlying skin, hence there is considerable destruction of the parenchymatous tissue. It is a great temptation to open such an abscess over its presenting point, but unfortunately this does not always give adequate drainage. Puddling of secretions with maceration of adjacent tissues prolongs the time required for healing and favors the formation of chronic sinuses.

Whether the abscess ruptures spontaneously or is opened over its presenting surface, an exploring finger should be introduced to break up all pockets and convert the multilocular abscess into a single cavity. If gently and cautiously executed, such a maneuver is very effective.

Auchincloss<sup>1</sup> maintains that if great care is exercised in breaking these friable partitions, much good can be accomplished. He insists that the finger should be carried radially, or parallel to the ducts, so that it will not rupture them. If one encounters strong bands or heavy septa, they should not be avulsed or broken as they may be large blood vessels, milk ducts, or healthy fibrous tissue trabeculae. Preservation of these structures facilitates healing; their destruction merely favors the spread of the invading pathogens. Gentleness always pays good dividends! While exploring the abscess one should determine its extent and depth, and if the external ostium does not provide adequate drainage, a counterincision should be made and a large rubber tissue drain inserted. (Fig. 5B.)

Battle and Bailey<sup>3</sup> emphasize that there need be no hesitancy in placing the drains through normal tissue. Bohler<sup>4</sup> agrees with them and advocates drainage of the midmammary abscesses by making a large dependent incision in the inframammary fold, carrying this up behind the breast until the dependent portion of the abscess is reached. It seems that such a plan needlessly exposes healthy tissue to contamination. Hobbs<sup>8</sup> appreciated this and attempted to minimize the insult by making a stab incision into the abscess and inserting a fenestrated rubber tube. Riché and Morgue-Molines<sup>14</sup> modified the Hobbs treatment by attempting repeated aspirations of the abscess with small needles. This method is effective if the inflammatory process is small and superficial, but if the needle has to penetrate much fatty tissue a secondary infection inevitably follows. Again, the contents of the abscess may be so viscid that they cannot be evacuated through a small needle.

After studying these problems, we have developed a simple but effective method of treating the medium size, uncomplicated intramammary and retromammary abscess. Not only is the simplicity of this method appealing, but the fact that it can be used for ambulatory patients enhances

its usefulness. The first step consists in aspirating the inflammatory mass to determine whether it has progressed to the stage

lizes the breast and collapses the abscess cavity. (Fig. 9.) The drain effectively removes any secretions which may form

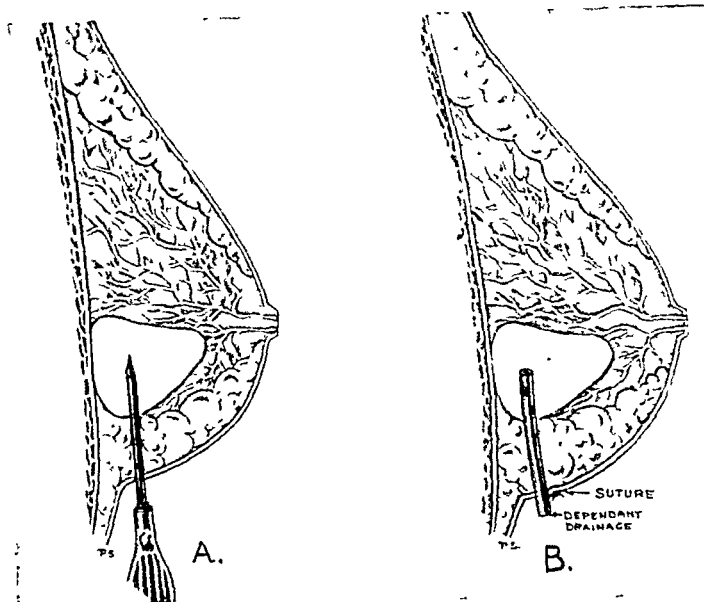


FIG. 8. A, insertion of the trocar into the abscess cavity. B, a fenestrated rubber catheter is inserted so as to afford dependent drainage.

of suppuration. (Fig. 5.) If so, the location of the abscess is studied and a point selected which will give dependent drainage. If possible this should be along the thoracomammary line. The skin and underlying normal tissues are infiltrated with novocaine and an incision 1 cm. long is made through the dermis only. A sharp-pointed trocar is plunged through the anesthetized area into the most dependent portion of the abscess cavity. (Fig. 8A.) After the obturator is withdrawn, a fenestrated catheter is inserted through the metal sheath and anchored to the skin with a dermal suture. (Fig. 8B.) The cavity is thoroughly lavaged with Dakin's solution. This primary irrigation is essential as it removes the inspissated pus and necrotic debris which might clog the catheter and inhibit proper drainage.

After the abscess has been irrigated thoroughly, the skin is covered with protective vaseline gauze and large absorptive fluffs are placed around the drainage catheter. A sponge pressure dressing is applied in such a manner that it immobi-

lizes the breast and collapses the cavity and heal. The pressure dressing should be

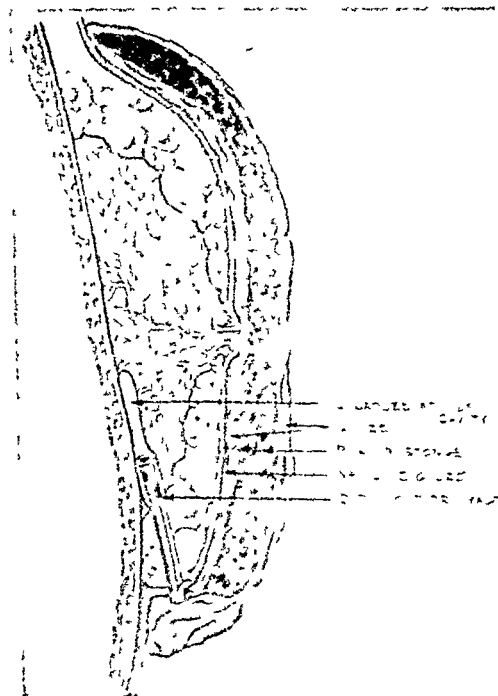


FIG. 9. Pressure sponge dressing.

applied in such a way that the absorptive fluffs can be readily removed when they

become soiled. This prevents maceration of the skin.

The simplicity of this method and its effectiveness are most pleasing, for at least 95 per cent of all midmammary and retromammary abscesses can be so treated. Unfortunately, however, it does have definite limitations. If the entire matrix is involved in a diffuse cellulitis or if there are multiple abscesses, more radical treatment, such as through and through drainage, may be required.

Regardless of the type of drainage employed, care must be taken to leave the drains in place until the deep abscesses have healed. A common error is to remove the drains just as soon as the discharge decreases, but the deep pockets may not be obliterated and if the ostium closes over, the abscess reforms. Residual infections and recurrent abscesses mean that the primary inflammation has not completely subsided. The average case requires drainage and irrigation for at least seven to ten days, and it should be observed closely for early signs of recollecting pus.

It is imperative that general systemic measures be employed to reinforce the surgical treatment. If possible, these patients should have complete rest, liberal diets high in caloric and vitaminic content, and frequent applications of short wave diathermy.

The breasts have great recuperative powers and if given a chance the destroyed tissues will be replaced by normal glandular substance. Fortunately, the diseased breast will assume its regular functions with the next lactation and as a rule there is only a slight decrease in the amount of milk which an affected gland will produce. The infrequency with which mammary abscesses are encountered is a tribute to the intelligent type of obstetrics being practiced today.

#### SUMMARY

1. The etiology, symptomatology and diagnosis of acute mastitis and breast abscesses are discussed.

2. A "caked" breast is not an acute inflammatory process but rather one of congestion.

3. The use of an aspirating needle is informative in differentiating the "caked" breast and the simple inflammatory mastitis from the suppurative variety.

4. Acute mastitis usually responds to conservative therapy and seldom terminates in suppuration.

5. Adequate surgical drainage is essential in the treatment of all types of mammary abscesses.

6. A simple but effective method of draining mid-mammary and retromammary abscesses by means of a trocar and catheter is described.

#### REFERENCES

1. AUCHINCLOSS, HUGH. Surgery of the Breast. In Nelson's Loose Leaf Living Surgery, Vol. 4, Chapter 1, 1937.
2. BAER, J. L., and REIS, R. A. Breast infections. *Surg., Gynec. & Obst.*, 32: 353, 1921.
3. BATTLE, R. J., and BAILEY, G. N. Treatment of acute intramammary abscesses by incision and by aspiration. *Brit. J. Surg.*, 23: 640, 1936.
4. BOHLER, E. L. Opération de la mastite puerpérale. *Bull. Soc. d'obst. et de gynec.*, 18: 269, 1929.
5. DAWSON, E. K. Histologic study of normal mamma in relation to tumor growth. *Edinburgh M. J.*, 42: 569, 1935.
6. DE LEE, J. B. The Principles and Practice of Obstetrics. Philadelphia, 1934. W. B. Saunders Co.
7. DIPPEL, A. L., and JOHNSTON, R. A. A suppurative mastitis as a complication of pregnancy and puerperium. *Am. J. Obst. & Gynec.*, 29: 258, 1935.
8. HOBBS, J. E. New method of treatment of breast abscesses. *Surg., Gynec. & Obst.*, 54: 839, 1932.
9. HUNT, H. B. Personal communication.
10. KLAHN, J. Mastitis and Stillfahigkeit. *Zentralbl. f. Gynäk.*, 61: 2059, 1937.
11. KEYNES. Quoted by Dawson.<sup>5</sup>
12. KILGORE, A. R. The Breast. In Dean Lewis' Practice of Surgery. Vol. 5, Chapter 6, pp. 6., Hagerstown, Md., 1937. W. F. Prior Co.
13. MOON, A. A., and GILBERT, B. Acute mastitis of puerperium. *J. Obst. & Gynec. Brit. Emp.*, 42: 262, 1935.
14. MORGUE-MOLINES. Quoted by Battle and Bailey.<sup>3</sup>
15. SHERRICK, J. W. Physiology and minor pathology of functioning breast. *California & West. Med.*, 34: 764, 1926.
16. WILLIAMS, W. R. Diseases of the Breast. London, 1894. John Bale & Son.

# A REGIME FOR CONTROLLING PAIN IN FAR ADVANCED CANCER PATIENTS\*

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MANY cancer patients require pain relieving drugs for several weeks or months. Sometimes narcotics are given in increasing doses, so that the continued excitation produced by the drug makes the patient more uncomfortable than the pain of the disease. In other cases insufficient sedation is given, and long weeks of suffering are endured—much of which might have been prevented.

The following régime has been evolved over a period of five years, during which time we have had 700 cancer patients, practically all of them in far advanced stages, under our care. The nursing unit is small, so that individual reactions and needs could be closely watched, and there was no need for routinization. The drugs discussed are only those we have used personally. Other common drugs undoubtedly have a field of usefulness in these cases, but either we have not found them necessary, they are too expensive, or we did not know of them.

## GENERAL NURSING CARE

A hospital bed, frequent changes of linen, avoidance of irritation of bony prominences, bodily warmth, simple care of the bowels, nourishing food (perhaps high protein content, adequate vitamin B because of the wasting of the disease) will make many patients comfortable. We mention this only because we have seen so many patients, who have required pain relieving drugs at home, become comfortable and require very little medication after they have had proper nursing care.

"If a cancer patient can get five to six hours sleep, and can take his food during the day, he is not suffering intolerable pain and the drug (morphine) need not be

increased." We have roughly followed this standard, laid down by Wild<sup>1</sup> of London. Though some authorities feel that there is no reason for sparing the use of morphine in these cases, we try whenever possible to limit the increase in narcotics, if the patient can possibly be kept comfortable by milder drugs.

## SEDATIVES AND ANALGESICS

Sedatives presumably act on the higher brain synapses, while the analgesics, because they decrease general sensitiveness of the body without depressing mental activity, are supposed to act on the lower centers, e.g., the thalamus. This is an explanation for the synergistic action of these two sets of drugs (Grabfield<sup>2</sup>).

*Sedatives (Soporifics).* Alcohol is perhaps the oldest hypnotic, dating back to early antiquity (Hjorst<sup>3</sup>). Cannabis indica (Indian hemp) opium, hyoscyamus, valerian and other medicinal herbs were known to the ancients. Later, came opium alkaloids. Next came naturally occurring inorganic chemicals: first bromine salts (potassium bromide, later sodium bromide), then magnesium compounds. Then came synthetic chemicals, chiefly inorganic: chloroform 100 years ago, and shortly afterwards its derivative chloral (1869), the first modern hypnotic, which swept into such immediate popularity that within two years 200 articles were written about it, and it was actually manufactured in tons. One chemist wrote that he produced and sold one half ton each week (Hjorst<sup>3</sup>). Paraldehyde, urethanes, methanes (trional, sulphonal) date from about 1880 to 1890.

The first *barbiturate* (barbital) was introduced in 1903 by Fischer under the

\* From the Mercy Hall Tumor Clinic and Hospital.

trade-name of veronal. Pharmacologic and clinical research since then has been concerned chiefly with an increasing number of commercially exploited barbiturates. Older drugs have lost popularity because of toxicity, or unpleasant properties, but there is much uncritical acceptance of newer remedies, and the virtues of some of the older drugs are being forgotten.

*Alcohol*, in addition to its hypnotic action, is a mild analgesic. It also produces peripheral dilatation and a sense of warmth and is an easily assimilated food (whiskey 2 or 3 drams every three or four hours, or 2 ounces of port wine at bed time). Wild<sup>1</sup> states that it has a synergistic action reinforcing other anodynes.

*Bromides* are the mildest sedative, useful for "pains all over," "hypersensitiveness." *Chloral hydrate* has fallen into disuse because of the objectionable taste and the danger of heart failure in large doses. Nevertheless it is still one of our most useful sedatives (Hjorst<sup>3</sup>), and in small doses there is little if any danger of heart failure (Grabfield<sup>2</sup>). In the compound elixir, chloral and potassium bromide, 1 dram contains 15 gr. each of chloral hydrate and potassium bromide plus extract of hyoscyamus gr.  $\frac{1}{8}$ .

Acetylsalicylic acid and aminopyrine (see analgesics) are sedative in addition to being analgesics (Fantus<sup>4</sup>). *Chloreton* (chlorbutanol), a chloral derivative, is locally anesthetic—to the gastric mucosa (gr. 5 to 20). It is a mildly useful sedative in nausea and vomiting (Beckman<sup>5</sup>). *Carbamides* combine ethyl, bromide and urea radicals. They possess greater sedation than bromides—standing midway between bromides and barbiturates (Carbromal, adalin, or bromural, gr. 10 to 20).

*Barbiturates* are derivatives of malonyl urea (barbituric acid), representing a large variety of combinations of alkyl, such as ethyl, groups plus malonyl urea nucleus (Lundy,<sup>6a</sup> Leake<sup>6b</sup>). Though some authorities differ, most consider that they are sedative only, and have no analgesic action except in very large doses which produce

deep narcosis. (Wagner<sup>7</sup>). Barbitol, the first synthesized, contains two ethyl groups plus malonyl urea. *Phenobarbital* (luminal) is a phenyl ethyl urea derivative. Barbitol and luminal are just as useful in these cases as the more complex proprietary barbiturates which are extensively advertised and they cost about one-thirtieth as much.

*Hyoscine* is useful for very excitable patients. There is considerable individual variation in the dosage required. Sometimes gr.  $\frac{1}{400}$  to  $\frac{1}{600}$  is ample, but, on occasion, as much as  $\frac{1}{50}$  gr. can be prescribed.

*Analgesics*. For pain relief we first use the coal tar drugs, all of which have analgesic action. They are also circulatory depressants. It is a general rule that if small doses do not relieve, larger ones are ineffective and may be toxic so that there is no advantage in increasing the dose. There are two groups: the analgesic antipyretics (acetanilid, acetphenetidin and aminopyrine) and the antirheumatic antipyretics (acetylsalicylic acid), so-called because they are thought to lessen the degree of inflammatory reaction in the fibrositis of rheumatic pains.<sup>8</sup>

Of the first group, acetanilid (gr. 3) is the least expensive, and though not used very frequently today, is "perhaps as safe as any of them" (Fantus<sup>4a</sup>). The danger of methemoglobinemia can be watched for. Acetphenetidin (phenacetin) gr. 5 is routinely prescribed. Aminopyrine, (pyramidon) gr.  $1\frac{1}{2}$  to 5 has three times the analgesic power of either acetanilid or acetphenetidin. Only a very occasional patient is sensitive to it, so that the danger of neutropenia is not great, but the white blood count should be observed occasionally, especially in sensitive (allergic) individuals (Watkins<sup>9</sup>).

Of the antirheumatic antipyretics acetylsalicylic acid (gr. 5 to 10) is probably the most useful analgesic we possess. Atropine, belladonna, and extract of hyoscyamus are prescribed with it to allay sweating and gastric irritation; and caffeine to avoid circulatory depression.

Combinations of these two groups of coal tar derivatives, the analgesics and the antirheumatics are very useful, for one obtains the synergistic action of two analgesics. Many extensively used and exploited popular commercial tablets contain this combination.

## COMPOUND ASPIRIN TABLET

	Gr.
Acetylsalicylic acid	3½
Acetphenetidin	2¼
Extract of hyoscyamus	⅙
	Gr.
Acetylsalicylic acid	3½
Acetphenetidin	2½
Caffeine...	½

Next, we add a sedative to the coal tar analgesic. Barbiturates are the most popular sedatives in these combinations today. "The barbiturate diminishes the patient's anticipation of pain, renders the patient more amenable to the analgesic action of the antipyretic." It does not reinforce the analgesic except in this fashion.

Popular combinations of barbiturates and coal tar drugs are:

	Gr.
Aminopyrine	3 to 4
Phenobarbital	½ to 1½
Compound Aspirin Tablet with phenobarbital	¼
Barbital	4
Acetanilid	1½

There is no satisfactory evidence that commercial mixtures of proprietary barbiturates and aminopyrine are any more valuable than these mixtures.

**A Warning.** The analgesic is eliminated faster than the barbiturate. Watch for cumulative action of the barbiturate if given over a long period of time. Toxic symptoms from long continued moderate doses are: *mental*—confusion, uncertainty, defects in attention and memory, diplopia; *skin*—urticaria, itching, scarlatiniform rash; *general*—anorexia, nausea, diarrhea, epigastric pain, thick speech, etc. (Lundy,<sup>6a</sup> Wagner<sup>7</sup>).

We have kept many patients comfortable until near the end on the above prescriptions. When they fail to give relief, we then resort to the opiates.

## OPIATES

First, we use codeine, gr. ¼, ½ or 1. Larger doses of codeine cause restlessness and excitement. Codeine is a weak narcotic, perhaps one-tenth as potent as morphine (Fantus<sup>1a</sup>).

Codeine may be added to the above prescriptions, as follows:

	Gr.
A.* Acetylsalicylic acid	2
Sodium bicarbonate	3
Atropine sulfate	⅓
Codeine sulfate	½
	Gr.
B. Acetylsalicylic acid	3½
Acetphenetidin	2½
Caffeine	½
Codeine	⅓, ¼ or ½*
	Gr.
C.*† Prescription B. but add:	
Codeine	1
Phenobarbital	1

\* Tablet #1, 2, or 3.

† Kaplan.<sup>10</sup>

The tablet can also be given orally, and the codeine by hypodermic administration. Dilaudid gr. ¼<sub>8</sub> is a good substitute here. It is cheaper than codeine and a more powerful analgesic. First give tablets during the day, and injections at night, or during rainy weather.

Some patients demand an injection. We have kept many comfortable by one of the above tablets plus injections of sterile saline solution—with perhaps stronger medication at night. If aspirin relieves by day, a milder drug than morphine will relieve at night (Daland<sup>11</sup>).

When the patient requires stronger narcotics, at first we give an occasional subcutaneous injection of morphine (gr. ⅙ to ¼), or dilaudid gr. ⅓<sub>2</sub> to ⅓<sub>20</sub>, or pantopon gr. ⅓. At this period suppositories of opium or dilaudid may be useful—they last longer (eight to ten hours) and par-ent-er-al administration is not needed.

But it is important at this time to search for other methods of relieving pain and discomfort. These depend largely on individual circumstances, but may include any of the following: control of anemia, dehydration, improvement of appetite; treatment of vitamin B<sub>1</sub> deficiency; care and



cleansing of wounds; drainage of cellulitis and abscesses; short circuiting alimentary canal operations or operations for similar threatened occlusion of the respiratory or urinary tract; treatment of urinary sepsis; suction drainage of urinary fistulas; alcohol intraspinal injection; peripheral nerve injection; cordotomy; x-ray therapy—especially for spinal metastases.<sup>12</sup>

A few cases will illustrate:

**CASE I.** An old man, age 78, had carcinoma of the left side of the mouth originating in the buccal mucosa near the ascending ramus of the mandible. Severe pain gradually developed in the left side of the face. The cheek became more swollen. Morphine injections every three to four hours were required.

Alcohol injection of the fifth nerve was about to be done, when an abscess broke beneath the mandible, with considerable relief.

**CASE II.** A man, age 68, had carcinoma of the bladder, and suffered from frequency, dysuria, and pain localized inside the rectum. He required opium or dilaudid suppositories three times daily. Two intraspinal injections of absolute alcohol, two weeks apart, relieved him so that there was frequency, but no dysuria, and the pain in the rectum was a mild "burning" coming occasionally.

**CASE III.** A colored woman had carcinoma of the cervix which had ulcerated into the bladder. Codeine and aspirin capsules every four or five hours were required for the discomfort and soreness caused by the discharges. Continuous suction, with a gauze wick in the vagina (Stedman pump, Hendrikson catheter)<sup>13</sup> kept her dry—the inflammation subsided, and she required only an occasional mild sedative at night.

Of 100 patients cared for at Mercy Hall until exitus, which included cancer of all types, with three months minimum observation,

47 per cent required only coal tar drugs and sedatives.  
33 per cent required narcotics the final two weeks only.  
20 per cent required narcotics for a longer period of time.\*

\* Daland<sup>11</sup> likewise commented on the small amount of morphine and codeine used at the Massachusetts State Cancer Institute at Pondville. An average of 3½ gr. of morphine per patient per month was all that was required, and this included operative care.

As morphine is stepped up, in the 20 per cent who need it, it is our practice to intersperse the doses as much as possible with the sedative and analgesic prescriptions above. Toward the end, in some cases, powerful sedatives are needed. Hyoscine (scopolamine) is used clinically for acute mania and excitement. It is frequently useful in the terminal stages, producing deep narcosis with peaceful oblivion. Occasionally there is idiosyncrasy; then it causes excitement.

Hyoscine and morphine have strong synergistic action. The familiar H.M.C. tablet contains the two drugs plus cactine, an old cardiac stimulant.

HMC	#1, Gr.	#2, Gr.
Hyoscine.....	½00	½100
Morphine.....	⅛	¼
Cactine.....	⅛20	⅛60

Schlesinger's solution is also a powerful synergistic combination. Though it has the advantage of being oral drops, we have not made extensive use of it because in our experience it frequently causes restlessness and excitement after use for a short time.

		10 minims =
Scopolamine HBR.	.005	⅛0 gr.
Morphine.....	.8	⅛ gr.
Dionin.....	.4	⅛ gr.
Water q.s.....	20.0	

Halsted used morphine and dionin orally (courtesy Dr. E. R. Arn, Dayton, Ohio).

Morphine.....	
Dionin.....	aa gr. viii
Aqua.....	q.s. Zi

Dose: 5 drops on sugar 2 or 3 times daily. Increase the dose as required.

The combination of morphine and chloral, the familiar "knockout drops" of the underworld, is simple, and again probably not used as frequently as it might be.

Morphine sulfate.....	0.15	Gm.
Chloral hydrate.....	15	Gm.
Fluidextract of Glycyrrhiza.....	30	Gm.
Syrup orange q.s.....	60	c.c. drams 1 (Fantus <sup>4</sup> )

Hyoscine may be added to this mixture.

Another combination we have found useful is trivalate, a powerful analgesic and sedative, which may have a long action, as much as twenty-four hours in some cases. It produces some euphoria also.

	Gr.
Caffeine valerate.....	$\frac{1}{17}$
Cocaine.....	$\frac{1}{12}$ —1 ampule
Morphine valerate.....	$\frac{3}{6}$

Cobra snake venom is a complex alkaloid which has a slower action than morphine, but it is more prolonged. One-half to one ampule every day, or every other day may keep a patient comfortable who otherwise would require an opiate every three to four hours. Its action is quite variable and unpredictable, however.

#### DISADVANTAGES OF MORPHINE

The disadvantages of prolonged morphine administration which we have encountered are: (1) it is habit forming—tolerance may be gained rapidly—within two to three weeks; (2) constipation is universal; (3) loss of appetite, nausea, vomiting are frequent; (4) there is euphoria—which, however is not always a disadvantage, but the patient is irritable, morose, depressed, nauseated, constipated. Increasing doses are necessary to control the discomfort, much of which is caused by the drug itself.

Dilaudid, although its action is similar, and prolonged usage does produce habit, has certain advantages over morphine in cancer patients. The appetite is retained. This is very important, for patients have less discomfort, feel better, therefore fewer drugs are required. Constipation is less frequent and less severe and hypnosis is less marked. This is better if the patient is ambulant at all. If hypnosis is desired, a barbiturate is added.

#### TREATMENT OF MORPHINE ADDICTION

A craving for morphine can develop within ten days after starting its use, but it usually takes three to four weeks to manifest itself. Often patients are given a box of morphine tablets to keep next to the bed at

home. Sometimes in general hospitals hypodermic injections of morphine are given freely and uncritically.

As stated earlier, we believe that it is distinctly worthwhile to take the patient off heavy morphine doses if it is at all possible to keep him comfortable otherwise. In cancer patients, addiction is due to the use of the drug for relief of physical pain and for this reason the habit is easier to break than in psychotic or constitutionally inferior groups, provided pain is relieved.

The methods of morphine withdrawal are:

1. Gradual daily reduction of morphine. Secure a good night's rest with phenobarbital, amytal, chloral hydrate, hyoscine. Gradually supplant morphine with codeine, aspirin, etc., as tolerated. Ashworth<sup>14</sup> states that if morphine is supplanted with pantopon, the change to codeine is easier. Use high caloric diet and large quantities of fluids. This treatment is sufficient for many of these cases.

2. Insulin may be used (units 10 to 12) in conjunction with the above gradual withdrawal, or morphine can be withdrawn completely, and insulin, units 10 to 30 substituted according to patient's discomfort and craving, increasing the dose (every two to four hours) until symptoms are relieved. One hundred sixty units or more may be given in twenty-four hours. Let the patient have a mild shock before giving food or sugar. Continue high dosage of insulin three days to one week, then as symptoms disappear, gradually discontinue the insulin, provided appetite and food intake are good. When the patient is taking small amounts of the drug, it can be withdrawn abruptly (Crowley<sup>15</sup>). Though the mechanism of the sparing action of insulin on morphine is not certain, it is believed that the adrenal function of carbohydrate metabolism is interfered with in morphinism (Piker, Crowley<sup>15</sup> and others).

3. Complete withdrawal, keeping patient somnolent forty-eight to seventy-two hours with sodium amytal gr. 3 to 6 every six to eight hours. Then give codeine,

aspirin, etc., sparingly for pain. We have found this method very useful in these cases. One must watch for barbiturate circulatory depression, especially in debilitated individuals.

4. The scopolamine—pilocarpine treatment described by Klingman and Everts.<sup>16</sup> We have not used this method. The patient is kept asleep for forty-eight hours with scopolamine gr.  $\frac{1}{200}$  given every one or two hours. This is then "washed out" with pilocarpine nitrate, gr.  $\frac{1}{8}$  for five hours.

When withdrawing morphine, one must be on the alert for withdrawal symptoms. Watch for restlessness, apprehension, vague discomfort, loss of appetite, yawning, generalized aches, pains, cramps. It is often difficult to tell whether the patient has real physical pain. If he is unable to localize his symptoms, will not take an oral tablet and insists on a needle, if medication relieves three hours by the clock and he then demands more at regular intervals, or if he will sleep for hours on an injection of physiologic salt solution plus 5 grains of aspirin, then "pain" is probably morphine craving.

Severer symptoms of morphine withdrawal are: tremors, perspiration, twitching, vomiting, diarrhea, palpitation. Usually, withdrawal symptoms subside if the patient can go three or four days without morphine.

#### SUMMARY

A regime for pain relief in far advanced cancer is described. Simple sedatives, coal tar analgesics, mild then stronger analgesics are used in increasing scale.

The importance of pharmacologic action, individualization of drug and patient, danger of overdosage, control of morphine addiction, consideration of methods other than drugs to relieve pain are emphasized.

#### REFERENCES

1. WILD, R. B. An address on the treatment of patients with inoperable cancer. *Lancet*, 2: 1062 (Nov. 24) 1928.
- 2a. GRABFIELD, G. P. Use of hypnotics. *J. A. M. A.*, 107: 1381, 1936.
- 2b. GRABFIELD, G. P. Observations on efficiency of commonly used hypnotics. *J. A. M. A.*, 96: 1865, 1931.
3. HJORST, A. M. Hypnotikon in H. A. Christian medical papers, p. 903. Baltimore, 1936. Waverly Press.
- 4a. FANTUS, B. Therapy of pain. *J. A. M. A.*, 103: 1939, 1934.
- 4b. FANTUS, B. Therapy of insomnia. *J. A. M. A.*, 102: 1846, 1934.
5. BECKMAN, HARRY. Treatment in General Practice, 3rd Ed., p. 608. Philadelphia, 1938. Saunders.
- 6a. LUNDY, J. S., and OSTERBERG, A. E. Review of literature on barbituric acid derivatives. *Proc. Staff Meet., Mayo Clin.*, 4: 386, 1929.
- 6b. LEAKE, C. D. Some pharmacologic aspects of pre-anesthetic medication. *Northwest Med.*, 29: 561, 1930.
7. WAGNER, C. P. Pharmacologic action of barbiturates. *J. A. M. A.*, 1787, 1933.
- 8a. SOLLMAN, T. A Manual of Pharmacology, 5th Ed. Philadelphia, 1936. Saunders.
- 8b. CUSHNY, A. R. Pharmacology and Therapeutics, 11th Ed. Philadelphia, 1936. Lea & Febiger.
- 8c. BASTEDO, W. A. Materia Medica, 4th Ed., 1937.
9. WATKINS, C. H. Possible role of barbiturates and amidopyrine in causation of leukopenic states. *Proc. Staff Meet., Mayo Clin.*, 8: 713, 1933.
10. KAPLAN, IRA I. Radiation Therapy. New York, 1937. Oxford University Press. p. 528.
- 11a. DALAND, E. M. Relief of pain in cancer patients. U. S. Public Health Service. Supplement 121 to Public Health Reports. Reprint #33.
- 11b. DALAND, E. M., and NATHANSON, I. T. The use of dilaudid in treating patients with cancer. *New England J. Med.*, 213: 741, 1935.
12. SALTZSTEIN, H. C., LAUPPE, E. H., and FELDSTEIN, M. Z. Care of advanced cancer exclusive of relief of pain by drugs. *Am. J. Surg.*, 48: 376, 1940.
13. SALTZSTEIN, H. C. A simple method for keeping dry bladder fistulas from cervix cancer. *Surg., Gynec. & Obst.*, 69: 111, 1939.
14. ASHWORTH, W. C. Ramblings about whiskey and drug addiction. *Virginia M. Monthly*, 58: 678, 1932.
- 15a. PIKER, P. Insulin in treatment for symptoms caused by withdrawal of morphine and heroin—report of 10 cases. *Arch. Neurol. & Psychiat.*, 36: 162, 1936.
- 15b. CROWLEY, R. M. Use of insulin in certain psychiatric disorders (bibliography). *Virginia M. Monthly*, 65: 678, 1936.
- 15c. HACKFIELD, A. W. Alcoholism and morphinism in private practice. *Northwest Med.*, 34: 7, 1935.
- 15d. CHEN, M. P., CH'ENG, Y. L., and LYMAN, R. S. Insulin treatment of drug addiction. *J. Nerv. & Ment. Dis.*, 83: 281, 1936.
- 15e. MODERN, F. S. Insulin in the treatment of chronic morphinism. *M. J. & Rec.*, 136: 163, 1932.
- 15f. HOWARD, M. Q. Treatment of morphinism with insulin: a preliminary report. *Wisconsin M. J.*, 32: 448, 1933.
16. KLINGMAN, T., and EVERTS, W. H. Intensive treatment of morphine addiction. *J. A. M. A.*, 106: 18, 1936.

# ANORECTAL ACTINOMYCOSIS\*

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**A**CTINOMYCOSIS, although commonly found in other parts of the body, rarely occurs in association with anorectal lesions. Illich, who reviewed 421 cases of actinomycosis in 1892, did not record any case in which the anorectal region was involved.

Sanford and Voelker studied 670 cases in 1925. The gluteal region was involved in five cases, the perirectal region in five cases, the scrotum in four cases, and the thigh, ovary, Fallopian tubes, both ovaries and Fallopian tubes, kidney, bladder, testes and penis, in one case each.

## ETIOLOGY

Although this disease is most frequently found among farmers, persons in all walks of life are susceptible. It is more common among males than among females. Several reasons for this have been considered: One is that men are more prone to exposure since most of the men who are infected are farmers; another reason is that mouth hygiene is not as good in men as it is among women. According to Sanford and Voelker, 80 per cent of those who have actinomycosis are males. It is distributed widely in the United States and is especially prevalent in the upper part of the Mississippi Valley and in the northwestern portion of this country. It is found at all ages, but most frequently affects young adults. Some observers say that *Actinomyces bovis* has not been found in persons free of the disease or elsewhere in nature. An organism simulating this one may inhabit the mouths of healthy persons but it is not believed to be pathogenic. In the collected series of cases of anorectal actinomycosis the youngest patient was a

girl aged 14 years, and the oldest a man aged 72.

## MODE OF INFECTION IN MAN

The mode of infection in man is disputed. Some say that the infection occurs through the agency of hay, straw, grass, and clover. Others contend that such substances furnish only the trauma which permits organisms, namely, actinomycetes which are normally present in the tonsillar crypts, carious teeth, and other regions, to display their pathogenic properties (Wright and Lord). Schlegel said that "actinomycetes are found in the body under normal conditions, but they do not possess sufficient virulence to produce trouble." He claimed that the disease usually begins as a fresh introduction of fungi. According to Kazda, the fungus is not able to produce disease unless there is local injury of tissue. Berestnew was able to isolate the actinomycetes from straw, grass and hay. New and Figi expressed the opinion that the prevalence of the disease indicates abundant organisms on the vegetation. Direct contagion from an infected animal to man or from man to man has not been definitely proved. Instances have been reported in which one person has bitten another who in turn has become ill with actinomycosis at the site of the bite. Naeslund, a Swedish bacteriologist, working in Upsala in 1925 and 1926, succeeded in isolating both the aerobic and anaerobic forms of actinomycetes from the human mouth. He claims that some of his anaerobic strains are identical with *Actinomyces bovis* which were obtained from human beings who had actinomycosis.

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Minges, in 1892, obtained "sulfur granules" from a patient and was able to infect a white rat by planting a single colony in

the history that the patient has used grass, straw or hay to cleanse himself following defecation.

#### LESIONS OF BONE ASSOCIATED WITH ANORECTAL ACTINOMYCOSIS

Primary involvement of bone in man is rarely if ever found and when observed it usually is the result of extension from an adjacent process. This is in contrast to the disease in cattle in which the jaw bone is the most frequent lesion. Langenbeck is said to have been the first one to observe the actinomycetes in a chronic disease of the vertebrae. This, however, is doubted by many observers today. Sanford and Magath expressed the opinion that the actinomycetes usually do not involve the bony structures of the human being. In the case reported by Perry there was destruction of the sacrum and in the one I am reporting there was involvement of the left side of the sacrum when the patient was seen in January, 1935. Roentgenographic studies of the pelvis revealed some irregularity of the inferior left aspect of the last segments of the sacrum. (Fig. 2.) In May, 1935, stereoscopic studies of the anteroposterior and lateral roentgenograms of the sacrum did not reveal any apparent change in the irregularity previously seen. Since that time, with improvement in the granulomatous reaction, the contour of the sacrum apparently has become more smooth and regular in outline, as demonstrated by the roentgenographic studies made in December, 1937. (Fig. 3.) This leads one to suspect that the lesions of bone accompanying actinomycosis in the human being may be the result of an osteomyelitis caused by secondary infection. When the actinomycetes are found in bone they may be coincidental. With arrest of the disease the lesion of bone appears to subside. Further study is necessary to clear up this observation.

The paucity of reports of anorectal actinomycosis in the literature and the finding of only one instance of this condi-

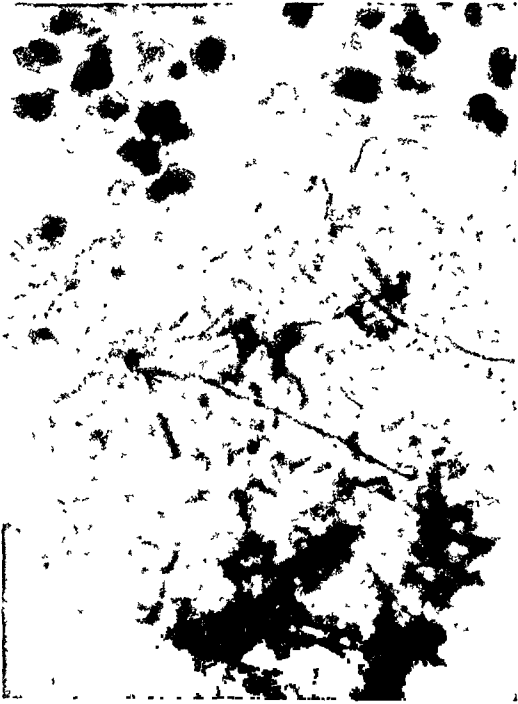


FIG. 1. Actinomycotic lesion in which the mycelia are shown very well; specimen stained with Gram's stain ( $\times 1150$ ).

the peritoneal cavity. This rat lived for eighteen months. Potassium iodide was fed in the milk. Later a nodule was noted on the jaw of the rat. Usually, however, attempts to inoculate laboratory animals are unsuccessful.

In cases of anorectal actinomycosis the organism (Fig. 1) usually is admitted through the mouth and migrates down the intestinal tract with the food until it reaches a region where stasis occurs. According to Hinglais, this commonly happens in the cecum and rectum. A small abrasion in the mucous membrane provides a portal of entry. The stomach and upper part of the intestinal canal usually are not involved. This has been explained on the basis that the organism does not grow well in an acid medium. The fungus may enter an abrasion of the perianal skin or it may enter infected or ulcerated crypts or other lesions at the anorectal outlet. In such instances it is often possible to learn from

tion among all of the cases in which proctoscopic examinations have been performed at The Mayo Clinic support the

inches (3.7 cm.) to the left of the anus. He had removed the head of this lesion, and a few drops of thick, yellow pus had escaped. During the



FIG. 2. Irregularity of inferior left aspect of the last segments of the sacrum; roentgenogram was made in January, 1935.



FIG. 3. Roentgenogram of same pelvis as shown in Figure 2. This roentgenogram, which was made in December, 1937, shows that the inferior left aspect of the sacrum is more regular in outline and smoother than it was in January, 1935.

idea that the anorectal region is rarely involved. I was able to find only one recorded case of anorectal actinomycosis in this country,<sup>25</sup> but on reviewing the foreign literature I found reports of sixteen cases<sup>1,2,4,6,7,11,18,24-29,33,36</sup> in which the condition might be considered to be anorectal actinomycosis, although the description was not always clear and the presence of primary actinomycosis of the anorectal type was not always established.

#### REPORT OF CASE

A man, aged 70 years, who was the manager of an oil company, came to the clinic, October 9, 1933, complaining of multiple fistulas around the anus. There had not been any evidence of tuberculosis. He had been in the habit of chewing clover. On occasions, while he had been in the oil fields, he had used leaves as a substitute for toilet paper. He always had enjoyed excellent health until 1919. Since that time, when he had been traveling on the trains, he often had found it necessary to shift about in the seat because of discomfort, which he described as "a feeling as if he were sitting on a broken spring." In 1920, he first had felt a soreness in the region of the rectum when walking. At that time, a small lesion, which he thought was a boil, had been discovered 1½

following years, the lesion had healed; pus had been discharged intermittently, but nothing had been done therapeutically until 1929, when he had consulted his family physician because of a similar lesion which had appeared near the first one. The second lesion had opened spontaneously, and it had been found that the two sinuses were connected. A rubber drain had been drawn through the tract between the two sinuses; this had been allowed to remain for several days. After the drain had been removed, the sinus 1½ inches to the left of the anus had healed in a few days but within a week it had broken down again and thick, yellow pus had been discharged continuously. In 1933, an attempt had been made to excise the sinus tract, but healing had not occurred.

Physical examination at the clinic disclosed that the man was well preserved. The pulse and temperature were normal; there was no pallor and the lungs were clear. Roentgenographic examination did not disclose any abnormality. Proctoscopic examination disclosed an indurated and inflamed mass in the left buttock; the mass contained two sinuses. One was situated 6 cm. to the left of the posterior margin of the anus, and the other was situated 4 cm. to the left of the anterior margin. (Fig. 4.)

The value for hemoglobin was 13.7 Gm. per 100 c.c. of blood. A flocculation test for syphilis was negative. The patient was advised to

to the left gluteal surface. The largest scar had several islands of granulation tissue at its base and there was another island of granulation

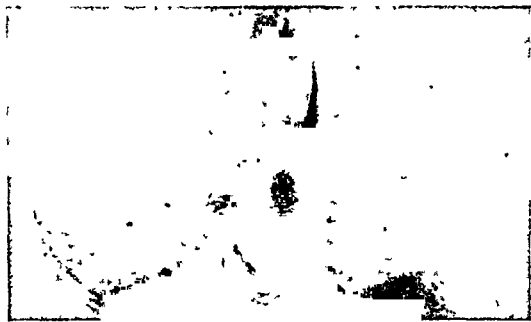


FIG. 4. Multiple, deep, anal fistulas associated with actinomycosis.

undergo an operation but he decided to postpone treatment.

He consulted another physician elsewhere in November, 1933, and at that time an operation was performed and five sinus tracts were found to communicate with the two openings previously described in the skin of the buttock. At the operation "all tracts were scraped," but the wound failed to heal. Approximately three months after the operation, and while the wound was being dressed, a probe was believed to come in contact with a bone, which was thought to be the coccyx. Another operation was performed elsewhere in November, 1934, but the coccyx appeared to be normal and was not disturbed. All efforts to stimulate healing failed and pus continued to drain from the wound. Pain and soreness soon developed in the left hip. This pain increased when drainage from the sinuses diminished, and was relieved when good drainage was established. Up to this time, the man had lost 20 pounds (9 kg.); he had noted moderate loss of sphincteric control ever since the first operation in 1933.

In December, 1934, a roentgenographic examination of the bony structure of the pelvis, which had been made elsewhere, had been thought to disclose osteomyelitis of the sacrum.

He returned to the clinic on January 17, 1935. When he was examined at this time, the temperature and pulse were normal. Moderate pallor of the skin and mucous membranes was noted. Fistulas were found in the left buttock, and diffuse redness, swelling, and increased local temperature were observed over the left greater trochanter. There also were several deep, linear scars which extended from the anus

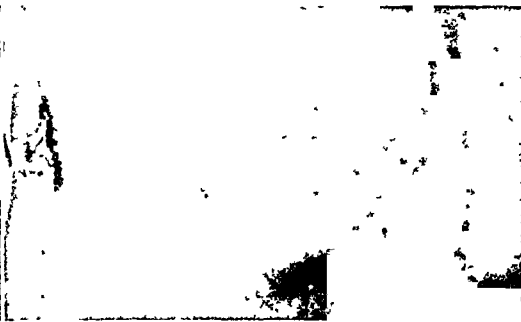


FIG. 5. Fistulas of left buttock in case of anorectal actinomycosis; photograph was taken shortly after a large abscess over the left hip had been incised and drained.

tissue at the base of another sulcus. A communication with the rectum could not be demonstrated. Proctoscopic examination disclosed a large crypt in the median line of the anal canal, posteriorly, but no tract was found extending toward the external sinuses. The left posterior wall of the anus was distorted by scar tissue.

The hemoglobin was 11.9 Gm. per 100 c.c. of blood; the erythrocytes numbered 4,030,000 per cu. mm., and the urine was normal. Roentgenographic studies of the pelvis, left hip, and femur revealed evidence of some irregularity of the sacrum. There was considerable thickening of the soft tissue overlying the left greater trochanter.

The abscess of the left buttock (Fig. 5) was incised on January 21, 1935. It contained a large quantity of pus and exuberant granulation tissue. At that time, specimens of tissue and pus were taken from the abscess cavity. The pathologist reported that the tissue was inflammatory, but "sulfur granules" (Fig. 6) were found in the pus. The tissue of the left side of the sacrum was examined.

The treatment consisted of incision and drainage of the abscess. Potassium iodide was administered in doses of 25 gr. (1.6 Gm.) three times a day. Administration of larger doses was attempted, but without success, because of the patient's intolerance. Gauze packs saturated with compound solution of iodine (Lugol's solution) were applied within the walls of the abscess and fistulas. Deep Roentgen therapy was administered.

The patient finally left the clinic February 22, 1935. At this time the iodine packs and

potassium iodide were still being used. He was advised to continue the deep Roentgen therapy elsewhere.

*Subsequent Course.* When the patient was heard from on June 13, 1935, he complained of diarrhea and generalized abdominal cramps. This was interpreted as a reaction which might follow high voltage Roentgen therapy. One month and two days later, the sinus over the left hip remained the same as it had been. It was packed daily with a piece of gauze moistened in a compound solution of iodine (Lugol's solution). The probe was inserted approximately 3 inches. The sinuses about the anus were very sensitive to the insertion of the probe and to irrigations with hydrogen peroxide. There was a constant dull ache in this region and a mass was present. The patient complained of generalized weakness and an occasional sharp pain in the region of the sacrum. Medication consisted of the oral administration of 50 gr. (3.3 Gm.) of potassium iodide three times a day.

When the patient was heard from again on October 28, 1936, the sinuses had healed. The one over the hip had healed two months before this date and the large one near the anus had healed a short time after the first one had healed. The sacrum remained the same as it had been. The administration of iodide had been discontinued in January, 1936. In six weeks the sinuses had started to drain. The administration of iodide was started again and since February, 1936, all the sinuses were "nearly half closed" and in October, 1936, there was only slight drainage. The sacrum still remained unchanged. The attacks of sharp pain about the sacrum had disappeared.

The patient was heard from again on February 16, 1938. The iodide had been used constantly except for brief intermissions, at which time the drainage from the sinuses had become more profuse than it had been and discomfort had been noted over the left hip and about the anus. Several times after the sinus on the left apparently had healed pain around the region of the left hip had been noted; this had been accompanied by swelling. A small soft spot had appeared and had been drained. A large amount of pus had drained from this region and "sulfur granules" were found. This sinus tract had been completely healed for five months, but near the anus there was another sinus tract which discharged a small amount of thin pus inter-

mittently. An applicator could be inserted 3 inches into this tract. This sinus, as well as the other, was treated by irrigations with hydrogen



FIG. 6. Exudate obtained when an abscess was incised; "sulfur granules" are visible.

peroxide, by using a small tube and a syringe. The sinuses then were packed loosely with gauze soaked in compound solution of iodine



(Lugol's solution). Medication consisted of 60 gr. (4 Gm.) of potassium iodide three times daily; this dose was increased to 80 gr. (5.2 Gm.) three times a day at intervals until symptoms of iodism appeared. The patient said that "these large doses of potassium iodide always helped to dry up the fistulous condition." A recent examination of the blood revealed the erythrocytes and leucocytes to be normal in number. A cholecystectomy had been performed in 1936 because of chronic cholecystitis and cholelithiasis. At that time the patient had lost 20 pounds (9 kg.) but this weight had been regained and the patient weighed 189 pounds (85.7 kg.), his normal weight. His health was rather good and he was in Oklahoma attending to business regularly. Roentgenographic studies of the pelvis, which had been made in December, 1937 (Fig. 3) had revealed that the lower segments of the sacrum were more smooth and regular in contour than they had been.

#### SYMPTOMS

The symptoms of anorectal actinomycosis may be general, local, or both. There may be weakness, malaise, fever, loss of weight, abdominal pain, nausea, vomiting and diarrhea. These symptoms may be accompanied by such signs as the growth of a tumor about the anus or rectum, or by one or more abscesses with draining sinuses. In some cases, anemia is prominent only after the disease becomes chronic. Local symptoms may include only painful defecation and the formation of a tumor mass about the anus or in the rectum and single or multiple fistulas-in-ano. Melena is not usually seen, although the vascularity of this granulomatous process is always striking at operation. A small furuncle about the anus may be present for many years. This may discharge intermittently and be noticeable only because of soiling of the undergarments. This sign was noted in the present case and in the case reported by Nové-Josserand. Associated with this sign is the history of the possibility of direct contamination by the use of leaves for cleansing after defecation.

Four phases of anorectal actinomycosis were described by Bensaude in 1933. The

initial phase consists of proctitis which is accompanied by fever, abdominal cramps and diarrhea or constipation. The second phase is one of woody infiltration; the third phase consists of the formation of abscesses and fistulas. The fourth phase consists of the complications. These may be of three types: (1) those which occur in situ, such as multiple deep fistulas, abscesses which may result in the formation of cavities, and stenosis of the anus or rectum; (2) those which occur by continuity, such as involvement of the pelvic viscera; and (3) those which occur at a distance, such as abscesses of the liver and septicemia.

#### DIAGNOSIS

The diagnosis of anorectal actinomycosis is based on the history of a chronic draining sinus or sinuses, physical and proctologic examinations, and the discovery of actinomycetes in the pus or tissues of the sinus or cavity. A specimen of the exudate (Fig. 6) is placed in a test tube with some water or physiologic solution of sodium chloride. The "granules" are isolated and placed on a glass slide in a drop of a 20 per cent solution of potassium hydroxide, crushed with a coverslip, and examined immediately with the low power objective of the microscope. If the actinomycetes are not found in this manner, specimens obtained by curettage or a section of the tissue obtained from the region of the abscess may be imbedded in paraffin and stained with Gram's stain or with hematoxylin and eosin. When these sections are cut and examined the organism and its characteristics may be observed.

#### DIFFERENTIAL DIAGNOSIS

Anorectal actinomycosis must be distinguished from such conditions as benign stricture, anal fistula, tuberculosis of the anorectal region, carcinoma, sarcoma, amebic dysentery, and lymphopathia venereum. The first five conditions may be distinguished from actinomycosis by the history or by examination of the exudate or a section of the tissue. If tuberculosis is

suspected and if the tubercle cannot be demonstrated and the microscopic picture is debatable, guinea pig inoculation must be resorted to. Amebic dysentery may be diagnosed by the history of moderate diarrhea, the passage of small amounts of blood in the stools; careful examination of a warm specimen of the stool may reveal *Endamoeba histolytica*.

#### PROGNOSIS

When actinomycosis is found in any part of the body, the prognosis should be very much guarded. In the anorectal region, the disease is equally as serious as it is in other parts of the body. In most of the cases reported in the foreign literature the patients either died in a short time or the outcome was not disclosed. In the reported cases the average duration of life after the patients consulted a physician was approximately one year. In the case reported by Perry the patient had lived fifteen months when he last was heard from. In the case reported in this paper the diagnosis of anorectal actinomycosis was made in January, 1935; when the patient was last seen in February, 1938, he was enjoying rather good health and was attending to business regularly. Death is usually the result of propagation of the mycotic process (Geissler), amyloid degeneration (Rotter), or septicemia which is caused by secondary infection (Poncet and Bartsch).

#### SECONDARY LESIONS

The perianal or perirectal tissues are usually involved, but as the disease progresses any structures about the pelvis may be vulnerable as the granulomatous process follows the line of least resistance. Fistulas may develop between the intestines and bladder or between the liver and intestines; the latter condition likely is the result of direct extension of an abscess of the liver that is secondary to the primary rectal lesion. There may be infiltration of the vesical and periprostatic cellular tissue. Occasionally, the Fallopian tubes, testes,

ovaries and appendix may be secondarily invaded by a primary anorectal lesion.

#### TREATMENT

Treatment usually is not followed by very gratifying results except in those cases in which the disease is recognized early and therapeutic measures are instituted before the process has become very extensive. There are at present only three general therapeutic measures which may arrest the disease, namely, operation, the use of iodides, and the use of irradiation. Since the organism is anaerobic, Wangenstein said: "Complete and wide excision of the involved tissue when possible should be performed as soon as the diagnosis is made." There are cases in which excision is either unwise or impossible, especially if considerable exploring or manipulation is necessary; in such cases there is danger of spreading the organisms to other parts of the body. In such cases incision should be made, the sinus tracts should be curetted thoroughly, and ample drainage should be instituted. When toxic symptoms are present, such as malaise, fever, nausea, and vomiting, they may be relieved by the drainage of the abscess or by the formation of a sinus. Iodides have been used in all types of granulomatous conditions and some improvement has been noted. Iodide is not a specific remedy for actinomycosis, but when administered in large doses it seems to assist in arresting the symptoms. At the present time the patient in the case I observed is taking between 60 and 80 gr. (4 to 5.2 Gm.) of potassium iodide three times a day and has taken this dosage since 1935. The sinuses partially dried up until the symptoms of iodism appeared but when he discontinued the iodides the sinuses reappeared. The sinuses were irrigated with hydrogen peroxide and then packed lightly with gauze saturated with compound solution of iodine (Lugol's solution). The skin around the sinuses must be carefully protected with vaseline gauze when the packs saturated with compound solution of iodine are used. This method of

treatment is usually carried out twice a day.

In addition to surgical measures and the oral administration of large doses of iodides, radiotherapy has been found useful. In cases of anorectal actinomycosis Desjardins advises treatment with high voltage Roentgen therapy. He uses from 400 to 500 Roentgens generated at a potential between 140 and 200 kilovolts and filtered through 6 mm. of aluminum or 0.75 mm. of copper depending upon the size of the patient. The number of pelvic fields should be between 4 and 6, and in addition one perineal field should be treated. The maximal improvement requires that the treatment should be repeated several times and that the dose and the scheme of irradiation should be varied. Kleesattel and Ingber have both indicated that Roentgen rays or radium has no effect upon the organism. Iser wrote: "The effects of x-ray treatment in actinomycosis are not explained by the action on the fungus, but on its habitat." One of these methods of treatment, when used alone, has not proved successful, but when all three are combined the results are better. Vaccines have not proved successful in the treatment of this disease.

#### SUMMARY

Anorectal actinomycosis is rare. The portal of entry of the actinomycetes is unknown although direct contamination of any anorectal wound by cleansing with leaves or grass may offer a direct contact for the actinomycetes. The lesions in bone are uncommon; they may be the result of the secondary infection that accompanies actinomycosis rather than the result of primary involvement of bone by the fungus. Seventeen cases of anorectal actinomycosis have been reported previously. The case reported in this paper brings the total number of cases in the literature to eighteen. The diagnosis depends upon the finding of the "sulfur granules" in the exudate obtained from one of the sinuses,

or on the microscopic examination of a specimen of tissue which has been stained with hematoxylin and eosin or with Gram's stain. There is no specific treatment for anorectal actinomycosis. Surgical drainage of the abscess with a minimal amount of manipulation, sufficient doses of potassium iodide, and a satisfactory regime of high voltage Roentgen therapy have proved satisfactory in allaying the symptoms in some cases.

#### REFERENCES

1. BARTSCH, G. H. Beitrag zur primären Aktinomykose des Mastdarmes. *Wien. klin. Wchnschr.*, 44: 170-172 (Feb. 6) 1931.
2. BENS AUDE, R. L'actinomycose ano-rectale primitive. *Presse méd.*, 1: 371-375 (March 8) 1933.
3. BERESTNEW. Aktinomykose und ihre Erreger. *Zentralbl. f. Bacteriol.*, 24: 706-708 (July) 1938.
4. DELORE, M. X. Actinomycose anale, périrectale et périvésicale. *Lyon méd.*, 88: 372-374 (July 10) 1898.
5. DESJARDINS, A. U. Personal communication.
6. GEISSLER. Casuistische Beiträge zur Aktinomykose des Menschen. *Breslau aerztl. Ztschr.*, 11: 58-61, 1889.
7. HESSE, G. Ueber Aktinomykose. *Deutsche Ztschr. f. Chir.*, 34: 275-307, 1892.
8. HINGLAIS, MANUEL. Essai sur l'actinomycose appendiculo-coecale (appendicite et typhlite actinomycosiques. *Lyon*. 1897. A. H. Storck.
9. ILLICH, ALBERTO. Beitrag zur Klinik der Aktinomykose. *Wien*, 1892. J. Safir.
10. INGBER, EDMONDO. Über die Radiumsensibilität des Actinomycespilzes. *Strahlen-therapie*, 28: 581-588, 1928.
11. ISER, S. Cited by Bensaude.<sup>2</sup>
12. KAZDA, FRANZ. Einiges über Aktinomykose, ihre Klinik und Therapie und neue therapeutische Bestrebungen. *Deutsche Ztschr. f. Chir.*, 156: 312-377 (July) 1920.
13. KLEESATTEL, HANS. Cited by Ingber.<sup>10</sup>
14. KÖNIG, FRITZ. Ueber Einstülpungsmethoden bei der Operation der Fistula colli congenita und die gelegentliche Anwendung bei einer Mastdarmfistel. *Arch. f. klin. Chir.*, 70: 1008-1014, 1903.
15. LANGENBECK. Cited by Israël, James. Neue Beobachtungen auf dem Gebiete der Mykosen des Menschen. *Virchows Arch. f. path. Anat.*, 74: 15-53 (Sept. 2) 1878.
16. LORD, F. T. A contribution to the etiology of actinomycosis. The experimental production of actinomycosis in guinea pigs inoculated with the contents of carious teeth. *Boston M. & S. J.*, 163: 82-85 (July) 1910.
17. LORD, F. T. The etiology of actinomycosis. The presence of actinomycetes in the contents of carious teeth and the tonsillar crypts of patients without actinomycosis. *J. A. M. A.*, 55: 1261-1263 (Oct. 8) 1910.

18. MELCHIOR, EDUARD. Ueber die Aktinomykose des Mastdarms. *Beitr. z. klin. Chir.*, 70: 722-744 (Nov.) 1910.
19. MINGES, G. Cited by Sanford and Voelker.<sup>31</sup>
20. NAESLUND, CARL. Studies of actinomyces from the oral cavity. *Acta path. et microbiol. scandinav.*, 2: 110-145, 1925.
21. NAESLUND, CARL. Studies of tartar formation. *Acta path. et microbiol. scandinav.*, 3: 635-677, 1926.
22. NAESLUND, CARL. Experimentelle Übertragung der Aktinomykose vom Menschen auf Versuchstiere mittels Reinkulturen der Actinomycesform Wolff-Israel (Act. Israël). *Acta path. et microbiol. scandinav.*, 6: 66-77, 1929.
23. NEW, G. B., and FIGI, F. A. Actinomycosis of the head and neck. A report of 107 cases. *Surg., Gynec., & Obst.* 37: 617-625 (Nov.) 1923.
24. NOVÉ-JOSSERAND, LÉON. Un cas d'actinomycose ano-rectale. *Lyon méd.*, 108: 989-990 (May 26) 1907.
25. PERRY, C. C. Actinomycosis of rectal origin. *Tr. Am. Proc. Soc.*, 1935, pp. 196-200.
26. PONCET, A. Actinomycose fessière d'origine rectale; vaste phlegmon actinomycosique de la fesse et de la partie postéroexterne de la cuisse gauche. *Gaz. d. hôp.*, 76: 325-330, 1903.
27. RISAK, ERWIN. Zur Klinik der Aktinomykose des Rektums. *Deutsche Ztschr. f. Chir.*, 205: 129-134 (July) 1927.
28. ROTTER. Vorstellung mehrerer Patienten mit Actinomykose. *Verbandl. d. deutsch. Gesel. f. Chir.*, 15: 105-112, 1886.
29. SAMTER, E. O. Ein Beitrag zur der Lehre von der Aktinomykose. *Arch. f. klin. Chir.*, 43: 257-351, 1892.
30. SANFORD, A. H., and MAGATH, T. B. The etiology and laboratory diagnosis of actinomycosis. *Minnesota Med.*, 5: 71-80 (Feb.) 1922.
31. SANFORD, A. H., and VOELKER, MINNA. Actinomycosis in the United States. *Arch. Surg.*, 11: 809-841 (Dec.) 1925.
32. SCHLEGEL. Cited by Bartsch.<sup>1</sup>
33. THÉVENOT, LÉON. De l'actinomycose ano-rectale. *Rev. de chir.*, 26: 250-268, 1902.
34. WANGENSTEEN, O. H. The rôle of surgery in the treatment of actinomycosis. *Ann. Surg.*, 104: 752-770 (Oct.) 1936.
35. WRIGHT, J. H. The biology of the microorganism of actinomycosis. *J. M. Research*, 13: 349-404 (May) 1905.
36. ZEMANN, A. Ueber die Aktinomylose des Bauchfelles und der Baueingeweide beim Menschen. *Med. Jahrbücher, Wien*, 1883, pp. 477-495.



# FRACTURE OF THE JAWS\*

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THE increasing incidence of fracture of the maxillary and mandibular bones may be ascribed to the accidents resulting from the more frequent use of the automobile. When more evident injuries involve other parts of the body there is a tendency to neglect examination of the facial bones. Moreover, every community does not have someone suitably trained to handle this type of bone injury. As a consequence of delayed or inadequate treatment, there is the possibility of permanent deformity. We should like to call attention to certain fundamentals in management, to describe simplified methods of fixation and to point out effective means of controlling complications. Such requisites are essential if good functional and cosmetic results are to be obtained.

## DIAGNOSIS

Fracture may be caused by violence of a direct or indirect nature. The sudden impact of a great force against the face, as in striking the steering wheel, the removal of neoplasms of the jaw and the removal of deeply imbedded teeth may be etiologic factors in producing injury. Osteomyelitis may be a predisposing cause of spontaneous fracture.

The diagnosis depends upon careful clinical examination which should be supplemented by an x-ray survey. There is the usual history of injury. The symptoms, broadly speaking, are similar to those accompanying fracture of the other bones of the body. There is local tenderness, swelling, ecchymosis, mobility of the parts and impairment of function. Traumatization of the branches of the fifth nerve frequently leaves a state of anesthesia of the areas innervated. This is especially true of the lower lip in cases of fracture of

the mandible. When teeth are present in both jaws, a commonly observed and most dependable sign is malocclusion.

The roentgenogram furnishes a valuable and convenient means of determining the location and type of fracture. However, there are certain regions of the jaws which are difficult to x-ray accurately. Either because of the inability to obtain the proper focus or to superimposition of the shadows of contiguous bones, there may result negative roentgenographic evidence. This is particularly true in fractures of the upper jaw and the neck of the condyle. The maxilla does not lend itself to such clear exposures as the opposing jaw. There is a tendency of the cranial bones to obscure and blur maxillary fractures. As a consequence, clinical evidence in diagnosing fractures of the maxilla is much more reliable. The routine practice of making two lateral jaw exposures of the lower jaw cannot be considered a complete survey. Too frequently, fractures at the midline and neck of the condyle are overlooked. Good details of the latter may be obtained by employing the same technique as used in views of the mastoid area.

## FRACTURES OF THE MAXILLA

Fractures of the maxilla are more likely to be comminuted than those of the mandible; therefore, facial asymmetry is more prone to follow. The presence of such associated injuries as crushed walls of the sinuses and fractured malar and nasal bones, demands that the treatment be a carefully planned and meticulous procedure. The injury may be as simple as involvement of part of the alveolar process or so extensive as to sever the maxillae from their attachment to the skull. The line of cleavage in transverse fractures may

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be through the antra or higher up through the orbital cavities. In both cases there is the tendency for the face to elongate, the

regions. Fracture of the ramus and its processes is not so rare as is believed. Injury to the neck of the condyle is often

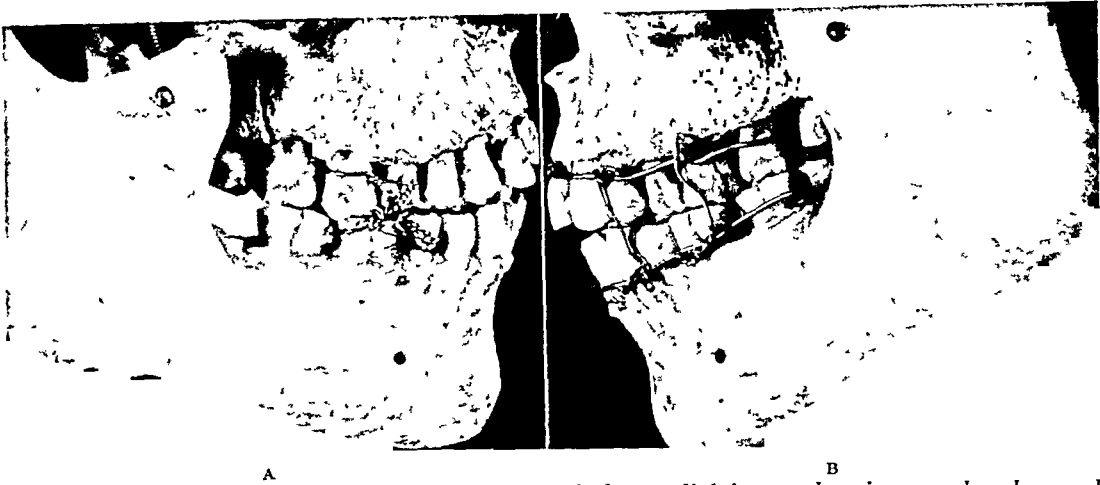


FIG. 1. A, Gilmer No. 1 method. Single wires twisted about adjoining teeth, crisscrossed and wound about wires similarly placed on occluding teeth. B, Gilmer No. 2 method. Heavy metal arch ligated by small wires to labial aspect of maxillary teeth.

whole of the dental arch being movable and held only by the soft tissues. Occlusion of the teeth is usually limited to the posterior parts of the jaws.

The treatment of fractures of the maxilla, except the transverse type, may be instituted by the various methods which will be dealt with in detail later. Complete fractures are best handled by exerting upward pressure on the jaw, utilizing the top of the head as a point of fulcrum. A dental splint is constructed and placed snugly about the teeth of the upper jaw which is carried gently to its former anatomic place by means of elastic traction. The exact position is gauged by establishing the previous occlusion of the teeth.

#### THE MANDIBLE

The lower jaw is more exposed to violence and is more often fractured than any other of the facial bones.<sup>1</sup> Fracture of the mandible may occur at any point from the symphysis to the glenoid cavity. Most often the body of the bone is involved especially at or near the angle. The second most frequently fractured site is in the region of the mental foramen. Double fractures commonly include both these

associated with fracture at the midline. Fractures of the body of the mandible are compound and therefore communicate with the mouth through the oral mucosa; those of the ramus are of the closed type. Injury to an edentulous mandible may be followed by extreme displacement of the fragments; because of the absence of teeth compounding of the fracture seldom results.

When consideration is given to the anatomic structure of the mandible, to the innumerable muscles to which it furnishes attachment, and to the opposing directions of pull, it is not surprising that fracture should so often be characterized by marked displacement. The treatment is dependent upon a knowledge of the musculature and of the various mechanical devices for fixation.

In a normally functioning jaw the muscles are in a fine state of balance. However, a break in the continuity of the bone upsets this equality of balance, producing traction of a greater degree in one direction than in another. Displacement is the obvious consequence. In a general way, unless prevented by the direction of the fracture line, upward pull is the result of the combined forces of the masseter,

temporal and internal pterygoid muscles; downward displacement is occasioned by the mylohyoid, digastric, geniohyoid and

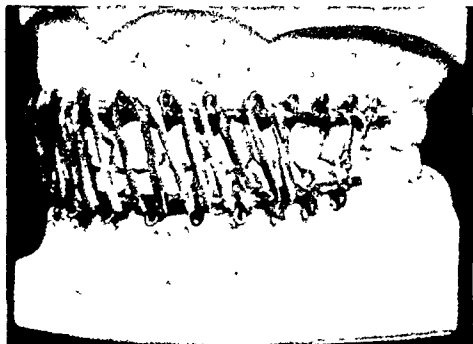


FIG. 2. The principle of elastic traction. Small elastics extended from maxillary to mandibular teeth, exerting constant pull.

genioglossus muscles. To overcome this condition of unbalanced action and to restore the parts to a state of equilibrium is a problem in dental mechanics.

#### TREATMENT

Treatment should accomplish two results: (1) bony union and (2) restoration of normal occlusion of the teeth. The achievement of the first objective without the other, will result in interference with the proper function of the mandible. It is for this reason that the reestablishment of the former relationship of the teeth assumes major importance. Moreover, normal occlusion is an ideal guide to correct reduction.

No two individuals possess exactly the same bite. There are, however, certain general conditions found in most mouths. The anterior teeth of the upper jaw usually overlap their antagonists of the mandible; the biting surfaces of the maxillary posterior teeth strike those of the lower jaw in such a manner as to incline slightly backward and to the side. A clue to the establishment of correct occlusion is furnished by noting the cusps which exhibit smooth surfaces as a result of wear. The articulation of these surfaces must closely approximate normal for the particular patient.

Various devices and procedures have been employed to effect reduction and fixation of fractured jaws. A brief discussion of each with an evaluation from a practical standpoint may be of interest.

**Bandages.** The Barton and other forms of head bandages are of little value as a permanent means of immobilization. In many cases their use is distinctly contraindicated. In simple fractures without disturbance of occlusion, the application of a bandage helps to afford a sense of security. Good results thus obtained may be attributed as much to the psychological effect on the patient as to the utilitarian value of the bandage. Today more cases are being seen which are characterized by comminution and extensive displacement. The use of a bandage in such cases not only fails to accomplish the desired results, but in reality tends to increase displacement. Should swelling of the soft tissues occur under a bandage, the pain and discomfort become intolerable. When used as a supplement to other forms of fixation, the bandage can be said to have reached the limit of its practical usefulness.

**Splints.** The use of splints for the purpose of reduction, except in special cases, is now considered unnecessary. The construction of metal and vulcanite splints is a time-consuming procedure which causes unnatural delay in instituting treatment.

**Metal Plates.** The placing of a piece of metal, such as the Lane plate, across the fracture line and attaching it by means of screws is now looked upon as an ill-advised and antiquated operation. Clinical experience has shown that frequently osteomyelitis develops.

**Direct Wiring.** The coaptation of the fractured parts by wiring one to the other is restricted to certain cases. It is indicated in fractures of edentulous jaws which do not lend themselves to other effective means of treatment. The facility of the intraoral approach and the fine results obtained have been recently emphasized.<sup>2</sup>

**Intraoral Ligation.** The simplest, the most universally employed and the most

satisfactory method of immobilization is obtained by the use of interdental wiring. Applicable in the vast majority of cases, it

each dental arch and held in place by fine wires which are ligated about several teeth. The jaws are brought into occlusion



FIG. 3. A, x-ray showing fracture of condyle of mandible with displacement. Malocclusion of teeth very pronounced. B, same case after reduction. Immobilized by Gilmer No. 2 method plus elastic traction.

possesses many advantages over other methods. It is a non-surgical procedure; occlusion of the teeth is always visible; it possesses none of the cumbersome characteristics of splints; opening the mouth for inspection does not materially disturb the relationship of the bone; and finally, it is neither irritating nor unhygienic.

Practically all types of wiring used in the present day treatment of jaw fractures are founded on the basic methods developed by the late Dr. Thomas L. Gilmer of Chicago.<sup>3</sup> Recognizing the fact that bringing the upper and lower jaws into occlusion was a practical way of not only properly approximating the parts, but of satisfying all the fundamental requirements essential to correct reduction, he devised two wiring methods which have become known as Methods No. 1 and No. 2.

The first method consists of twisting separate strands of 22-gauge brass wire about the necks of the adjoining teeth, crisscrossing the wires and winding them to wires similarly attached to the occluding teeth. When applied to the bicuspid and molar teeth of each side in addition to the anteriors, the result is that the two jaws can be closed in proper position.

The second method is indicated when several teeth are missing. A 14-gauge arch wire is fashioned to the labial aspect of

by intermaxillary tie wires which join the upper and lower metal arches. Thus the basic principle of establishment of the normal occlusion is carried out.

These two methods may be used over a wide range. However, many modifications of each have been made. The Ivy eyelet method is a very satisfactory device. It possesses advantages of both Gilmer methods.

The excellent results obtained in reduction by utilizing elastic traction prompts us to call attention to a phase of treatment, which, though far from being novel, is sometimes overlooked. In badly displaced cases reduction becomes a procedure of constantly tightening the intermaxillary wires until the process is completed. It is, to say the least, unpleasant from the patient's viewpoint. However, when small elastics are attached to the upper and lower wire hooks or projections, gradual and painless reduction immediately starts and often is completed within a few hours' time. It is particularly effective in late treated cases in which fibrous union has taken place. Permanent fixation is easily obtained by later substituting fine wires for the elastics.

There are certain types of fractures of the mandible which, because of problems in management, deserve special mention. Fractures occurring at the angle leave an



edentulous posterior fragment which exhibits a tendency to "ride up" and eliminate the usual space between both

#### COMPLICATIONS

The early complications such as hemorrhage and respiratory embarrassment usu-

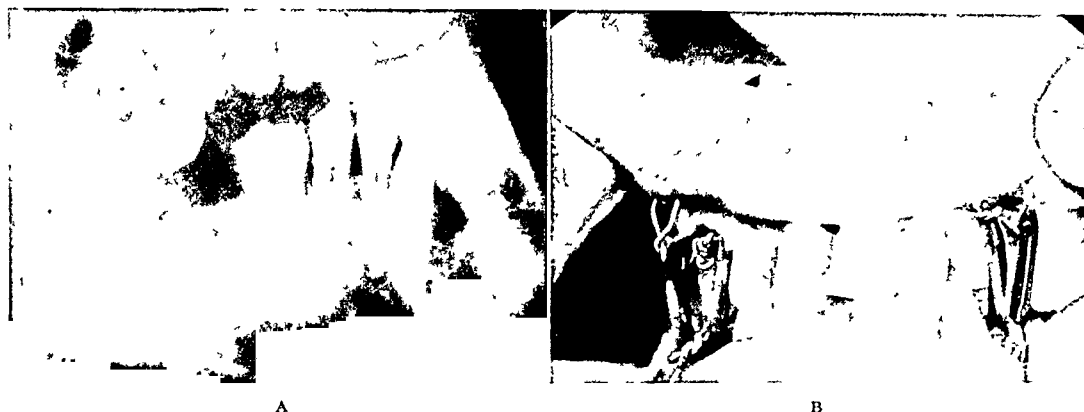


FIG. 4. A, x-ray showing fracture at angle of the lower jaw with ramus elevated. B, same case after reduction.

jaws. Union in these cases can only be obtained by using some mechanical means to place the elevated part back in contact with the larger fragment. A vulcanite splint fitted over the alveolar ridge of the fractured area usually is an effective solution of the problem. Fracture of an edentulous mandible is best treated by utilizing the patient's artificial dentures; reduction is completed by using an external elastic bandage. In badly displaced cases direct wiring or the circumferential method of Black are indicated.<sup>4</sup>

The management of fracture of the neck of the condyle has occasioned a great deal of comment and discussion. When displacement of the head of the process occurs there is a deviation of the midline to the side of the injury. Operations have been suggested to remove the condylar head because of fear of ankylosis. Such procedures present hazards and difficulties. It is worthy to note that in most cases clinical results obtained by wiring the upper and lower teeth in occlusion and disregarding the displaced condyle, have been most satisfactory.<sup>5</sup> The temporomandibular joint possesses the faculty of adjusting itself to the new condition. Therefore, the conservative treatment as here outlined is advocated.

ally disappear after reduction has been carried out. Late complications are cellulitis, osteomyelitis, malunion and nonunion. When swelling progresses to the stage of suppuration, incision of the soft tissues, providing an adequate vent for the pus, may prevent infection of the bone. Prolonged suppuration is indicative of osteomyelitis. This condition demands that ample drainage be established and maintained and sequestra be removed when separated from live bone. In a case complicated by infection of the bone osteogenesis is slower. Delayed union may result from failure to immobilize early, incorrect approximation of the fragments, the interposition of fibrous tissue and such general diseases as syphilis, tuberculosis and diabetes. Malunion invariably may be traced to improper reduction. Nonunion is comparatively rare. Restoration of the continuity of the jaw can only be obtained by resorting to bone grafting.

#### SUMMARY

1. More frequent use of the automobile has tended to increase the incidence of fracture of the maxilla and mandible.
2. Diagnosis depends on both clinical and x-ray examination.

3. Treatment should be directed toward obtaining bony union and restoring the normal occlusion of the teeth.

4. The maintenance of ample drainage and removal of sequestered bone are fundamental to the control of complications.

#### REFERENCES

1. BLAIR, V. P. *Surgery and Diseases of the Mouth and Jaws*. St. Louis, 1920. C. V. Mosby.

2. KAZANJIAN, V. H. Fracture of the edentulous mandible. *Apollonian*, 146: 148 (July) 1937.
3. GILMER, T. L. A case of fracture of the lower jaw with remarks on the treatment. *Arch. Dent.*, 4: 388 (Sept.) 1887.
4. DOHERTY, J. A. Fractures of the mandible and maxilla. *New England J. Med.*, 216: 425-428 (March 11) 1937.
5. DOHERTY, J. L., and DOHERTY, J. A. Fractures of the jaws and treatment. *Surg., Gynec. & Obst.*, 64: 70 (Jan.) 1937.



INTUBATION is the process by which a hard-rubber tube is introduced into an edematous and occluded larynx through the glottis. It is generally done in cases of laryngeal diphtheria in which the larynx has become so swollen as to threaten asphyxiation.

# DIAPHRAGMATIC HERNIA IN CHILDREN\*†

## A RÉSUMÉ OF SIXTY-EIGHT CASES OCCURRING IN CHILDREN UNDER TEN YEARS OF AGE TREATED BY OPERATION

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THE surgical repair of diaphragmatic hernias in infants and young children is still a relatively uncommon surgical procedure. With the advances made in roentgenology during the past fifteen years, many more diaphragmatic hernias are diagnosed during life than formerly, and with the progress made in the technique of anesthesia and thoracic surgery, a great many more cases have been successfully operated upon.

Hedblom<sup>1</sup> has written a most comprehensive discussion covering the whole subject of diaphragmatic hernia, and has collected 2,137<sup>2</sup> cases, including 629 cases of the esophageal hiatus type. Rankin and Grimes<sup>3</sup> have written a brief but excellent review, discussing in considerable detail the history of the development of the operation itself. Harrington<sup>4</sup> has reported 120 cases of various types upon which he has operated. Over 700 articles touching various phases of this subject have appeared in the literature during the past ten years.

Only an occasional author, however, reports an operation on a patient under ten years of age. A recent report by Truesdale<sup>5</sup> lists fifty such cases. Orr and Neff<sup>6</sup> have collected seventeen congenital cases under one year of age. Lissowetzky,<sup>7</sup> in the course of 220 routine autopsies on infants, found three congenital diaphragmatic hernias. In each case it had been the cause of death. He believes that, could an early diagnosis be made and surgical repair resorted to, the lives of many such cases

might be saved. Greenwald and Steiner<sup>8</sup> collected eighty-two cases of diaphragmatic hernias in infants and young children reported from 1912 to 1929. Only eleven, however, were operated upon, and only six of these survived. They also stress the importance of an early diagnosis. In the newborn infant the prognosis is poor, death being due chiefly to cardiac and pulmonary interference, as shown by the attending cyanosis and dyspnea. In older children the prognosis is better. Here intestinal obstruction and strangulation is the most common cause of death. In their series of eighty-two cases, forty-six were diagnosed at autopsy. Most of these were young infants. It is probable that, had they been diagnosed early and repaired, some of these would have survived. Woolsey<sup>9</sup> reported 106 cases collected from the literature. Thirty-six of these were in infants and children under ten years of age, in which diagnosis was not made until the autopsy was performed. He feels that in 71 per cent of his entire group of fatal cases, had an early diagnosis been made and operation performed, death might have been averted.

Diaphragmatic hernias are considered to be true or false, depending upon the presence or absence of a sac. Harrington<sup>4</sup> has classified them as follows: "a non-traumatic diaphragmatic hernia may be congenital or acquired.

"1. If congenital, the hernia is attributable to embryologic deficiency, and usually is without an enclosing sac. The most

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common sites in the probable order of frequency of occurrence are: (1) through the hiatus pleuroperitonealis (foramen of Bochdalek); (2) through the dome of the diaphragm; (3) through the esophageal hiatus; (4) through the foramen of Morgagni; (5) through the gap left by the partial absence of the hemidiaphragm which is usually in the posterior portion of the muscle.

"2. If acquired after birth, the sites of occurrence are: (1) through the esophageal hiatus—this type has an enclosing sac; (2) through the region of fusion of the anlage of the diaphragm; (3) at sites named under congenital types.

"3. Traumatic diaphragmatic hernia may be caused by direct or indirect injury, or by inflammatory necrosis of the diaphragm. (1) In indirect injury to the diaphragm, the hernia may occur at any point, including points of embryologic fusion, but the most common region is the dome and posterior half of the left hemidiaphragm—it may occur in the right hemidiaphragm. It is usually the result of a severe, crushing injury and the hernia may or may not have a hernial sac. When the hernia is through the esophageal opening there is a sac, but when through the leaf of the diaphragm, there is usually no sac. (2) In direct injury to the diaphragm, the hernia may occur at any point, and is usually the result of penetrating wounds, such as those inflicted by a gunshot or a knife. (3) Rupture of the diaphragm may be the result of inflammatory necrosis, which in turn has been caused by a subdiaphragmatic abscess or rupture may follow necrosis from drainage tubes introduced into empyema cavities. In these cases the opening in the diaphragm is usually posterior and there is no hernial sac."

We have reviewed sixty-eight cases of diaphragmatic hernia occurring in infants and children ten years of age or under which have been treated by operation. (Table 1.)

In this series of sixty-eight operated cases ten years of age or younger there were twenty-two deaths a total mortality



FIG. 1. X-ray twenty-four hours after injury, showing air-containing viscera in left thorax and absence of left diaphragm shadow.

of 32 per cent. Nineteen patients died shortly after operation, that is, before leaving the hospital, and are classed as operative deaths. Three died after leaving the hospital, one two months later, and the second six months later of recurrence which resulted in obstruction. In neither was a second operation done. In the third case the hernia recurred in six months, and the patient died after a second operation for repair. These three cases are classed as deaths in this tabulation. There were two more recurrences, making a total of five (7.4 per cent). These two patients were operated on again. One made a satisfactory recovery and has remained well. In the other case the hernia recurred twice more and following the third operation has remained well. Twelve cases showed definite signs of obstruction on admission. Eight of these died. There were fourteen cases in which the hernia was definitely attributable to a traumatic injury, and although these are acquired cases, they are differentiated in this paper by listing them separately as traumatic cases. There are only four non-traumatic cases which we

can be certain were definitely acquired. In three of these cases the hernia appeared following an empyema, in the fourth it appeared while the patient was convalesc-

The incidence is higher in males than in females, and the mortality slightly lower. Hedblom<sup>1</sup> found in 197 cases of all ages, that 78.6 per cent were males, and 24.4 per

TABLE I.  
RESUME OF 68 CASES OF DIAPHRAGMATIC HERNIA IN CHILDREN UNDER 10 YEARS OF AGE TREATED BY OPERATION.

NO	YEAR	REPORTED BY	AGE SEX	ETIOLOGY	DOMINANT SYMPTOM	HOW DIAGNOSED	APPROACH	CONTENTS	LOCATION	ANESTHESIA	RESULT	REMARKS
1	1889	O'DWYER <sup>18</sup> U.S.A.	3 YR. ?	CONGENITAL	DYSPEA OBSTRUCTION FEVERIOS	BY OPERATION	THORACIC	STRANGULATED INTESTINE AND COLON	LEFT	NOT RECORDED	DIED	DIAGNOSED EMPYEMA PUS PRESENT
2	1896	MAYLARD <sup>19</sup> SCOTLAND	8 YR. M.	CONGENITAL	VOMITING PAIN IN LF HYPOCHONDIUM ABDOMINAL DISTENTION	BY OPERATION	ABDOMINAL	STRANGULATED COLON AND OMENTUM	LEFT	NOT RECORDED	DIED	COLON RETURNED TO ABDOMEN. DIAPHRAGM NOT REPAIRED
3	1902	AUE <sup>13</sup> GERMANY	9 YR. M.	ACQUIRED APPEARED 1 YR. AFTER EMPYEMA	VOMITING PAIN IN LEFT SHOULDER	PHYSICAL FINDINGS	ABDOMINAL	PART OF STOMACH	LEFT MEDIAL	NOT RECORDED	LIVED	WELL 18 YRS AFTER
4	1917	MC CLEAVE <sup>15</sup> U.S.A.	31 MO. M.	CONGENITAL	PAIN RELIEVED BY VOMIT- ING DYSPEA CYANOSIS	X-RAY	ABDOMINAL	INTESTINES	LEFT POST.	NOT RECORDED	DIED	OPERATED BY DR L P ADAMS
5	1918	DOWNS <sup>14</sup> U.S.A.	7 YR. M.	CONGENITAL	VOMITING FAILURE TO GAIN WEIGHT	X-RAY	ABDOMINAL	STOMACH PART OF DUODENUM	LF ESOPH. HIATUS	INTRATRACHEAL	LIVED	STOMACH COULD NOT BE WITHDRAWN FROM THORAX POST. GASTRO JEJUNOSTOMY
6	1919	DE BUISS <sup>15</sup> U.S.A.	3 MO. F.	CONGENITAL	DYSPEA OBSTRUCTION COLIC UNABLE TO SWALLOW OR VOMIT	BY OPERATION	ABDOMINAL	STOMACH COLON OMENTUM	LEFT POST.	ETHER	DIED	
7	1920	GREWE <sup>16</sup> U.S.A.	5 YR. F.	CONGENITAL	VOMITING CONSTIPATION COUGHING	X-RAY	ABDOMINAL	STOMACH	LF. ESOPH. HIATUS	NOT RECORDED	LIVED	WOUND DISRUPTION 7TH PQ DAY - RECOVERED AUTHOR THINKS NOT ACQUIRED
8	1920	SPEIK <sup>17</sup> U.S.A.	5 YR. M.	CONGENITAL	SYMPTOMS OF PYLORIC ULCER, PARTIAL INTESTINAL OBSTRUCTION	BY OPERATION	ABDOMINAL	STOMACH	LEFT	NOT RECORDED	LIVED	
9	1920	AUE <sup>13</sup> GERMANY	5 YR. M.	CONGENITAL	VOMITING NAUSEA AFTER MEALS WEIGHT 14 LB.	X-RAY	ABDOMINAL	STOMACH COLON APPENDIX	RIGHT ESOPH. HIATUS	ETHER	DIED	OPERATED BY PROF. HEDBLUM - RECURRENT DIED 2 MO. POST OP.
10	1921	TRUESDALE <sup>18</sup> U.S.A.	5 YR. M.	TRAUMATIC RUN OVER BY AUTO	NAUSEA CHOKING SPELLS DYSPEA	AUSCULTA- TION X-RAY	THORACIC	MOST OF GLTRACT SPLEEN LF LOBE LIVER	LF PARA ESOPH. HIATUS	POSITIVE PRESSURE GAS O. ETHER	LIVED	RECURRENT 3 TIMES REOPERATED LIVED
11	1921	TRUESDALE <sup>19</sup> U.S.A.	3 YR. M.	TRAUMATIC RUN OVER BY AUTO	SHOCK	X-RAY	ABDOMINAL	STOMACH JEJUNUM TRANS. COLON LF LOBE OF LIVER	LF DONE SMALL TEAR IN RT.	POSITIVE PRESSURE	LIVED	OPERATED BY O'CONNELL
12	1921	ODETSCH <sup>10</sup> U.S.A.	8 YR. F.	TRAUMATIC STRUCK BY AUTO	NAUSEA DYSPEA PAIN	X-RAY	THORACIC	STOMACH COLON	LF. DONE INTRATRACHEAL	ETHER OXYGEN	LIVED	ALSO REPORTED BY GORDON AND GOLAN <sup>21</sup> PERSONAL COMMUNICATION
13	1921	BARNETT <sup>22</sup> ENGLAND	8 MO. ?	CONGENITAL	VOMITING CYANOSIS OBSTRUCTION ABD. DISTENTION	BY OPERATION	ABDOMINAL	STOMACH TRANS. COLON INTESTINE SPLEEN	LF DONE ABSENT	NOT RECORDED	DIED	OPENING COULD NOT BE CLOSED
14	1922	LEPOUTRE <sup>23</sup> FRANCE	3 MO. F.	CONGENITAL	DYSPEA CYANOSIS AFTER FEEDING UNDER WEIGHT	X-RAY	COMBINED	STOMACH ILIUM COLON	LEFT	NOT RECORDED	DIED	ARTIFICIAL RESPIR MASSAGE OF HEART DURING OPERATION
15	1924	BEHREND <sup>24</sup> U.S.A.	8 YR. M.	ACQUIRED EMPYEMA 5 MO. BEFORE	VOMITING PAIN CONSTIPATION	X-RAY	ABDOMINAL	STOMACH TRANS. COLON OMENTUM	LEFT CENTRAL	LOCAL	LIVED	OBSTRUCTED IVO. P.Q. REOPERATED LIVED
16	1924	GARMAN <sup>25</sup> U.S.A.	5 YR. F.	TRAUMATIC RUN OVER	ATTACKS ABD. PAIN DIS- TENSION BELCHING WORSE WITH EXERTION	X-RAY	THORACIC	SMALL INTESTINE OMENTUM SPLEEN	LEFT CENTRAL 12 CM LONG	POSITIVE PRESSURE NITROUS OXIDE O.	DIED	BECAME CYANOTIC DIED 10 HOURS AFTER OPERATION BY DR A HEDBLUM

ing from influenza. We have listed as congenital, all non-traumatic hernias where we cannot be quite certain that they were acquired.

cent females. Greenwald and Steiner<sup>8</sup> found 68.9 per cent males and 31.1 per cent females in their series. In forty-one cases the sex was not recorded.

Many other symptoms and physical findings besides those listed in Table III occurred, such as: malnutrition, anemia, choking spells, difficulty in nursing or

seen from this tabulation that under 1 year of age, cyanosis, dyspnea, and vomiting are the most common findings, while over one year, vomiting, pain and colic are the

17	1924	CARMAN <sup>11</sup> U.S.A.	9 YR. M.	CONGENITAL	LEFT ABDOMINAL CRAMPS FOR 1 YEAR	X-RAY	ABDOMINAL	MOST OF GI TRACT SPLEEN	LEFT CENTRAL	ETHER	DIED	OPERATED BY DREXSTAM JUDG
18	1925	SHERWOOD <sup>12</sup> U.S.A.	8 YR. M.	TRAUMATIC HIT BY TRUCK	TENDERNESS RIGIDITY UPPER ABD. - SHOCK	X-RAY	ABDOMINAL	STOMACH OMENTUM LF LOBE OF LIVER	LEFT CENTRAL	NITROUS OXIDE ETHER	LIVED	FRACTURE OF THE 7TH, 8TH, 9TH AND 10TH RIBS
19	1926	TRUESDALE <sup>13</sup> U.S.A.	8 YR. F.	TRAUMATIC COASTING	INTESTINAL OBSTRUCTION	EXPLOR. LAPAROTOMY	COMBINED	TRANS. COLON OMENTUM	LEFT FORAMEN BOCHALEK	POSITIVE PRESSURE GAS O <sub>2</sub> ETHER	LIVED	THREE FAILURES AFTER LAPAROTOMY
20	1927	WOOLSEY <sup>14</sup> U.S.A.	33 DA. F.	CONGENITAL	DYSPEA CYANOSIS	X-RAY	ABDOMINAL	SMALL INTESTINE COLON APPENDIX OMENTUM	LEFT POSTERIOR	NOT RECORDED	LIVED	DIED OF VOMITING 1 YEAR LATER HERNIA O.K.
21	1927	JOWERS <sup>15</sup> ENGLAND	7 YR. M.	ACQUIRED	VOMITING PAIN	PRELIMINARY EXPLOR. LAPAROTOMY	ABDOMINAL	ALL SMALL INTESTINE MOST OF COLON	LF DIAPH. DETACHED AT BORDER	INTRATRACHEAL O <sub>2</sub>	LIVED	FIRST SYMPTOM OCCURRED WHEN PT. WAS CONVALESCING FROM INFLUENZA
22	1927	SCHACKELTON <sup>16</sup> U.S.A.	9 YR. M.	TRAUMATIC OCCURRED WHILE WRESTLING	SUDDEN SEVERE UPPER ABD. PAIN DYSPEA SHOCK	X-RAY	THORACIC	STOMACH COLON SPLEEN OMENTUM	LEFT POSTERIOR	NITROUS OXIDE O <sub>2</sub>	LIVED	NOT POSITIVE PRESSURE ANESTHESIA PERSONAL COMMUNICATION
23	1927	STEPHENS <sup>17</sup> AUSTRALIA	5 YR. F.	CONGENITAL	VOMITING DYSPEA CYANOSIS	X-RAY	THORACIC	MOST SMALL INTESTINE CECUM APPENDIX	LEFT POST.	INTRATRACHEAL ETHER	DIED	DIED 6 MO LATER FROM OBSTRUCTION FROM 2ND DIAPHRAGMATIC HERNIA
24	1927	STEPHENS <sup>18</sup> AUSTRALIA	3 MO. M.	CONGENITAL	CYANOSIS CONVULSIONS "WINDY ATTACKS"	X-RAY	THORACIC	PART STOMACH, MOST SMALL INTESTINE, COLON CECUM AND APPENDIX	LEFT VENTRO LATERAL	INTRATRACHEAL ETHER	LIVED	
25	1927	CLARK <sup>19</sup> U.S.A.	3 YR. F.	CONGENITAL	VOMITING - ABDOMINAL PAIN - SENSE OF FULLNESS IN STOMACH	X-RAY	THORACIC	STOMACH PART OF SMALL INTESTINE COLON AND SPLEEN	LEFT ANTERIOR OF DOME	NOT RECORDED	DIED	PARA GASTRIC ABSCESS BROKE AT OPERATION
26	1927	TORRE <sup>20</sup> U.S.A.	4 YR. M.	CONGENITAL	NAUSEA CONSTIPATION ABDOMINAL CRAMPS AFTER EATING	X-RAY	ABDOMINAL	MOST OF STOMACH SMALL INTESTINE AND COLON	ESOPH. HIATUS LF NO SAC	GAS O <sub>2</sub> ETHER	DIED	ALSO REPORTED BY LEOPOLD <sup>21</sup>
27	1928	TRUESDALE <sup>22</sup> U.S.A.	5 YR. F.	TRAUMATIC HIT BY AUTO	CYANOSIS - COUGH	X-RAY	THORACIC	STOMACH SMALL INTESTINE COLON SPLEEN	LEFT PARA ESOPH.	POSITIVE PRESSURE GAS O <sub>2</sub> ETHER	LIVED	
28	1928	PAUCHET <sup>23</sup> LIQUET FRANCE	3 YR. F.	CONGENITAL	VOMITING PAIN CONSTIPATION	X-RAY	ABDOMINAL	STOMACH PART OF COLON	LEFT ESOPH HIATUS	NOT RECORDED	LIVED	
29	1928	OLMSTEAD <sup>24</sup> U.S.A.	6 MO	CONGENITAL	DYSPEA CYANOSIS LOSS OF WEIGHT	X-RAY	ABDOMINAL	INTESTINES SPLEEN	LEFT CENTRAL	ETHER	DIED	THORACENTESIS BEFORE DIAGNOSIS
30	1928	MEYER <sup>25</sup> U.S.A.	FEW WKS. M.	CONGENITAL	VOMITING, SYMPTOMS OF INTESTINAL OBSTRUCTION	X-RAY	ABDOMINAL	PART OF SMALL INTESTINE AND COLON	LEFT	NOT RECORDED	DIED	ASPIRATED VOMITUS DIED ON TABLE
31	1929	BETTMAN <sup>26</sup> AND HESS U.S.A.	3 MO. F.	CONGENITAL	DYSPEA CYANOSIS PAIN REFUSED FOOD	PERCUSSION AUSCULTA- TION X-RAY	COMBINED	INTESTINES COLON	LEFT LATERAL	POSITIVE PRESSURE ETHYLENE CO <sub>2</sub> O <sub>2</sub>	LIVED	
32	1929	MCFADDEN <sup>27</sup> IRELAND	4 YR. F.	CONGENITAL	VOMITING PAIN CONSTIPATION	X-RAY	THORACIC	INTESTINES COLON, SPLEEN OMENTUM	LEFT ANTERIOR	NOT RECORDED	LIVED	
33	1929	BROWN <sup>28</sup> U.S.A.	5 YR. F.	CONGENITAL	COLICKY PAIN	X-RAY	ABDOMINAL	STOMACH INTESTINE SPLEEN	LF ESOPH TO LAT. CHEST WALL	NITROUS OXIDE O <sub>2</sub> ETHER	DIED	
34	1930	SANDERS <sup>29</sup> U.S.A.	5 YR. F.	ACQUIRED EMPYEMA 3 YRS. BEFORE	ABD. PAIN NAUSEA VOMITING	X-RAY	COMBINED	PART OF STOMACH TRANS. COLON ENTIRE OMENTUM	LEFT POST.	POSITIVE PRESSURE ETHYLENE	LIVED	

swallowing, emptiness of abdomen, refusal of feedings, belching, diarrhea. Many of these could probably be included under the more frequently listed terms. It will be

most common complaints. This agrees with the findings of Greenwald and Steiner.<sup>8</sup> Under one year the dominant symptoms are the result of cardiac and pulmonary

embarrassment, while over one year, they are the result of a partial obstruction of the gastrointestinal tract.

involved; dextrocardia; dulness to flatness on percussion on the side involved; absent or diminished breath sounds on the in-

TABLE 1 (CONTINUED)

NO.	YEAR	REPORTED BY	AGE SEX	ETIOLOGY	DOMINANT SYMPTOM	HOW DIAGNOSED	APPROACH	CONTENTS	LOCATION	ANESTHESIA	RESULT	REMARK
35	1930	TRUEDALE <sup>18</sup> U.S.A.	1 YR. F.	CONGENITAL	REFUSED FEEDING DIGESTIVE UPSET CRYING SPELLS	X-RAY	THORACIC	STOMACH SPLEEN	LF ESOPH. HIATUS NO SAC	POSITIVE PRESSURE GAS O <sub>2</sub> ETHER	LIVED	
36	1930	TRUEDALE <sup>18</sup> U.S.A.	17 MO. F.	CONGENITAL	ABDOMINAL PAIN OBSTRUCTION DISTENSION COUGH	X-RAY	THORACIC	STOMACH COLON SMALL INTESTINES	LEFT FORAMEN BOCHDALEK	POSITIVE PRESSURE GAS O <sub>2</sub> ETHER	LIVED	CECOSTOMY 1 WK. BEFORE
37	1930	SCHONBAUER WARKANT <sup>22</sup> GERMANY	3 MO. ?	CONGENITAL	VOMITING DYSPEA COUGH LOSS OF WEIGHT	X-RAY	COMBINED	PART OF STOMACH ALL SMALL INTESTINE MOST COLON, SPLEEN	LEFT DOME	ETHER	LIVED	
38	1930	HARRINGTON <sup>41</sup> U.S.A.	7 MO. F.	CONGENITAL	SEVERE VOMITING OBSTRUCTION PROSTRATION	X-RAY	ABDOMINAL	ENTIRE STOMACH LARGE AND SMALL BOWEL	LEFT FORAMEN BOCHDALEK	ETHER ETHYLENE INTRATRACHEAL	DIED	PERSONAL COMMUNICATION
39	1930	HARRINGTON <sup>41</sup> U.S.A.	3 YR. M.	CONGENITAL	VOMITING	X-RAY	ABDOMINAL	PORTION OF STOMACH	LF THRU ESOPH. HIATUS	ETHYLENE	LIVED	PERSONAL COMMUNICATION POS. PRESSURE ANESTHESIA ALWAYS AVAILABLE IF NEC.
40	1931	DONOVAN <sup>42</sup> U.S.A.	4 MO. M.	CONGENITAL	DYSPEA CYANOSIS PAIN CONVULSIONS	X-RAY	ABDOMINAL	SMALL INTESTINES TRANS. COLON SPLEEN	LEFT POST.	POSITIVE PRESSURE ETHER	LIVED	PERSONAL COMMUNICATION
41	1931	BETTMAN AND HESS <sup>43</sup> U.S.A.	9 MO. F.	CONGENITAL	VOMITING DYSPEA COLICKY PAIN	X-RAY	COMBINED	SMALL INTESTINES	LEFT DOME	POS. PRESSURE ETHYLENE O <sub>2</sub> ETHER	LIVED	
42	1931	EGGERS <sup>44</sup> U.S.A.	4 WKS. F.	CONGENITAL	DYSPEA CYANOSIS PAIN WEIGHT LOSS	X-RAY	ABDOMINAL	STOMACH PART OF COLON - SPLEEN TIP OF LIVER	LF. LARGE EVEN- TRATION	GENERAL	DIED	TIP OF LIVER COULD NOT BE WITHDRAWN. LEFT IN
43	1931	ROBB <sup>45</sup> U.S.A.	7 WKS. M.	CONGENITAL	DYSPEA CHOKED WHEN NURSING	X-RAY	ABDOMINAL	STOMACH SMALL INTESTINES MOST OF COLON	LEFT POST.	NOT RECORDED	LIVED	OPERATED BY DR. S. WYATT
44	1931	CORTLOS <sup>46</sup> U.S.A.	13 DA. F.	CONGENITAL	VOMITING DYSPEA CYANOSIS	X-RAY	COMBINED	MOST OF G.I. TRACT SPLEEN	LF POST. FORAMEN BOCHDALEK	INTRATRACHEAL O <sub>2</sub> ETHER	LIVED	
45	1931	HIPPLEY <sup>47</sup> AUSTRALIA	10 YR. F.	CONGENITAL	VOMITING ATTACKS OF ABD. PAIN	X-RAY	ABDOMINAL	HALF STOMACH IN SAC	LF ESOPH. HIATUS SAC	OPEN ETHER	LIVED	PHRENIC N. CRUSHED
46	1931	UNSHLM <sup>48</sup> GERMANY	9 MO. M.	CONGENITAL	VOMITING MALNUTRITION ANEMIA	X-RAY	ABDOMINAL	STOMACH SPLEEN	LEFT ESOPH HIATUS	CHLOROFORM ETHER	DIED	
47	1931	STEPHENS <sup>49</sup> AUSTRALIA	6 YR. M.	CONGENITAL	VOMITING PAIN DIARRHEA	X-RAY	THORACIC	SMALL INTESTINES COLON SPLEEN	LEFT LATERAL POST.	INTRATRACHEAL ETHER	LIVED	
48	1932	JOHNSON AND BOWER <sup>50</sup> U.S.A.	41 HR. M.	CONGENITAL	DYSPEA CYANOSIS OBSTRUCTION	X-RAY	COMBINED	COLON AND OMENTUM	LEFT DOME	ETHER	LIVED	
49	1932	IZUKA AND SANO <sup>51</sup> JAPAN	8 MO. F.	CONGENITAL	VOMITING DYSPEA CYANOSIS	X-RAY	ABDOMINAL	MOST OF G.I. TRACT	LEFT POST. LAT.	LOCAL	LIVED	
50	1932	LAUENSTEIN <sup>52</sup> GERMANY	9 MO. M.	CONGENITAL	VOMITING CONSTIPATION OBSTRUCTED 8 DAYS	X-RAY	ABDOMINAL	MOST OF SMALL INTESTINES	LEFT	NOT RECORDED	DIED	

A word should be said here regarding the diagnosis. In any case showing the above symptoms, the physical examination may reveal tympany on percussion of the side

involved; râles, diminished excursion on the involved side, retraction of the abdomen; an epigastric mass; a rapid heart beat.





small and unusual type of eventration, the other three were deficiencies in the diaphragm. It is interesting to note that several patients were treated for considerable periods of time for other conditions, and a correct diagnosis was not made until x-ray studies had been completed. In five of the eight cases where the x-ray was not used, the diagnosis was definitely missed.

TABLE II

Male—37 54.4 Per Cent		Female—28 41.2 Per Cent		Sex Not Recorded—3 4.4 Per Cent	
Lived	Died	Lived	Died	Lived	Died
27 72.9 per cent	10 27.0 per cent	18 64.2 per cent	10 35.7 per cent	1 33.3 per cent	2 66.7 per cent

TABLE III  
RELATIVE FREQUENCY OF SYMPTOMS

Symptom	Entire Series 68 Cases	Trau- matic 14 Cases	Congenital and Acquired Cases		All Cases over 1 Yr 44 Cases
			Over 1 Yr 30 Cases	Under 1 Yr 24 Cases	
Vomiting	34	3	19	12	22
Dyspnea	24	5	2	17	7
Pain-colic	24	6	12	6	18
Cyanosis	18	2	1	15	3
Obstruction	11	2	7	2	9
Constipation	7		5	2	5
Loss of weight	7		3	4	3

If one could be certain before operation that a congenital deficiency of the diaphragm was present, it would probably be better to treat the case expectantly than to attempt repair. Of the three cases with diaphragmatic deficiencies reported in this series, two died and one was successfully repaired. LeWald<sup>61</sup> reports three cases of congenital absence of the left half of the diaphragm. He believes the condition does not lend itself to surgical repair. Beckman<sup>62</sup> reports a case of supposed diaphragmatic hernia operated by W. J. Mayo in 1909. A large deficiency was found, no repair was attempted. The patient recovered. Hume<sup>63</sup> believes congenital absence of the left half

of the diaphragm is usually incompatible with life.

It is generally felt also, that eventrations should not be operated upon. Clopton<sup>64</sup> reports two cases of eventration. He states diagnosis may be made by fluoroscopic and x-ray studies. The diaphragm moves with respiration, though less than normally, due to hypoplasia of the left lung. It may be confused with situs transversus from the fact that the heart is on the right side. The stomach will be on the left side, however. Lateral x-ray and fluoroscopic studies are particularly valuable. From this angle the diaphragmatic dome may be visible. He feels the prognosis is good under medical management, and that surgical measures should not be attempted.

Hume's<sup>63</sup> patient, a 6 year old boy struck by a truck, was not operated upon. A left thoracentesis was performed, and air and brown fluid obtained (presumably gas and intestinal contents). The patient died a few hours later, and necropsy revealed a left diaphragmatic hernia with the stomach, colon and omentum in the left thoracic cavity. The author believed this to be a congenital hernia. The child was almost moribund, and there is little question that nothing could have altered the fatal outcome. With the sudden and sometimes almost overwhelming respiratory and cardiac embarrassment which may follow such a traumatic injury, a massive thoracic hemorrhage, effusion, or a tension pneumothorax might have to be considered.

A thoracentesis was performed on Reiss's<sup>65</sup> 3 year old patient, and upon the twenty-two month old infant reported by Giustinian.<sup>66</sup> Death followed shortly afterward in each instance. Three taps were made in Brush's<sup>67</sup> case and twelve in De la Vega's<sup>68</sup> before the diagnosis was made. In one case in this series, reported by Olmstead,<sup>34</sup> a thoracentesis was performed before the diagnosis was made. Later, after the diagnosis had been made by x-ray, an operation for repair was performed.

The diagnosis is sometimes difficult, as has been well brought out by the researches

of Woolsey,<sup>9</sup> and Greenwald and Steiner.<sup>8</sup> Physical examination is often difficult and will not always reveal the real trouble.

condition may often be improved and anemia overcome by frequent small feedings, blood transfusions, etc. (4) General



FIG. 2. Preoperative x-ray showing absence of left diaphragm shadow and barium-filled small intestine in left thorax with gas-filled stomach above.



FIG. 3. Twenty-four hours postoperative. Note diaphragm shadow on the left side and left pneumothorax. The mediastinum has shifted to the right. There is no evidence of any abdominal viscera in the thorax. The small stomach catheter is still in place.

From a study of this series of cases, we feel the necessity of early and adequate roentgenologic study cannot be too strongly emphasized.

Since the first operation to be performed on a child nearly fifty years ago, the mortality has gradually decreased. This change has been largely due to several definite factors: (1) Earlier correct diagnosis, which means in substance improvement in roentgenologic technique, and the more frequent use of the x-ray. (2) Improvement in the anesthesia, i.e., better and less toxic anesthetic agents, better methods of administration, the simple closed method and the intratracheal tube which allows the anesthetist to administer positive pressure when the need arises. (3) Adequate preparation of the patient for the operation, which is now less often performed as an emergency measure. The patient's general

improvement in the technique has been derived mainly from those who have pioneered in this field.

The following are some of the advances which aid us in the correct handling of these cases. (1) The lavaging of the stomach by passing a small tube preoperatively, as stressed by W. Meyer,<sup>35</sup> is important. In the presence of a diaphragmatic hernia the stomach may not empty readily, and a retention may be present. With the replacement of the stomach in the abdomen, some of the gastric content may regurgitate, and be aspirated by the patient. (2) The crushing of the phrenic nerve, as advocated by Harrington,<sup>69</sup> aids in the repair by supplying a quiet and relaxed diaphragm. (3) The introduction of a stomach tube into the thoracic cavity via

the abdominal incision and the hernial opening in the diaphragm, as first advocated by C. H. Mayo,<sup>70</sup> allows air to be

thorax postoperatively does much toward relieving the cyanosis and dyspnea which follows the shift of the heart and the

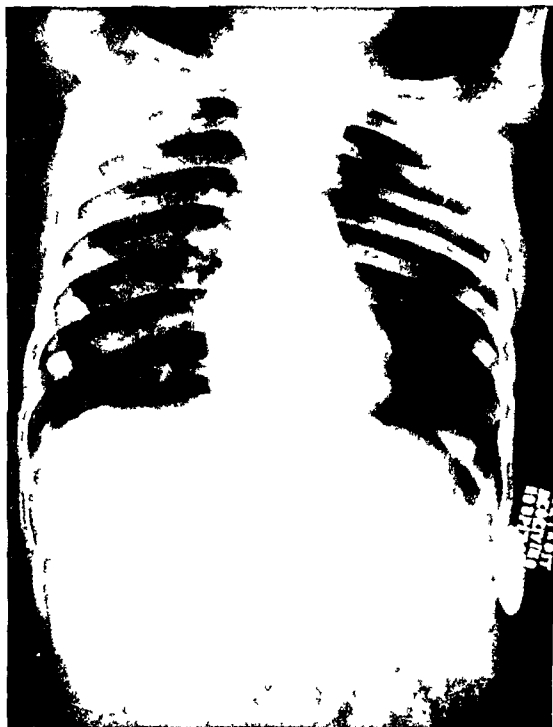


FIG. 4. One week postoperative. Complete outline of left diaphragm shadow but still about 60 per cent collapse of the left lung.

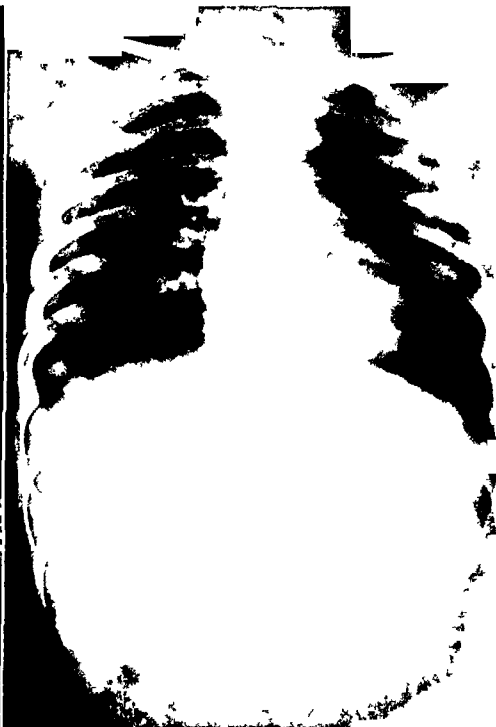


FIG. 5. Two weeks postoperative. Complete diaphragm outline and almost complete expansion of left lung visible.

introduced above the viscera, and destroys the suction which may make their withdrawal difficult. (4) The cutting or breaking of the ribs (first advocated by C. H.

mediastinum to the unaffected side at the time of the operation.

We believe the abdominal approach is usually the best. It seems reasonable to state that no one would favor the combined approach unless necessity demanded it. In children where the hernia has usually not been present for a long period of time, and where adhesions between the displaced abdominal viscera and the parietal pleura are rarely encountered, the abdominal approach seems more simple. Harrington's<sup>4</sup> enviable record of 120 cases of all types and ages, with ten deaths (mortality 8.3 per cent), seems to bear this out. However, in this series the mortality is definitely higher in those cases operated on by the abdominal route. It is unquestionably true that in a statistical study on such a small series of cases, and in one embracing a long period of years, there is grave danger of drawing false conclusions. However, a study of

TABLE IV

Years	No. Cases	No. of Deaths	Per Cent Mortality
1889-1920	9	5	55.5
1921-1930	23	11	47.8
1931-1938	36	6	16.7

Mayo,<sup>70</sup> Carrington,<sup>71</sup> Harrington,<sup>72</sup> and recently described by Bird<sup>58</sup>), may aid in the repair. If the diaphragm is torn from the chest wall, or if the opening cannot be closed because of tension, this procedure will relax the diaphragm sufficiently to provide enough tissue to accomplish the repair. (5) The aspiration of the pneumo-

these cases would lead one to suppose that the higher mortality encountered in the group operated on via the abdominal

administer positive pressure anesthesia, the hernia repair may be attempted. The truth of this statement would seem to be



FIG. 6. Fifteen days postoperative.

approach might be partially explained by the fact that from 1889 to 1920 only nine cases reached operation. The mortality during these years was nearly three times as great as during the past decade, and all but one of these patients were operated on via the abdominal route.

It is of vital importance to have a correct diagnosis before subjecting the patient to operation. In those cases where the diagnosis was not made preoperatively, and where the surgeon proceeded with the repair of the hernia after discovering it at the time of an exploratory operation, the mortality (80 per cent), is exceedingly high. If a diaphragmatic hernia is found during an exploratory laparotomy, it would seem to be good judgment to close the abdomen without repairing it. Then, at a later date, with adequate preparation, a blood transfusion and an anesthetist equipped to

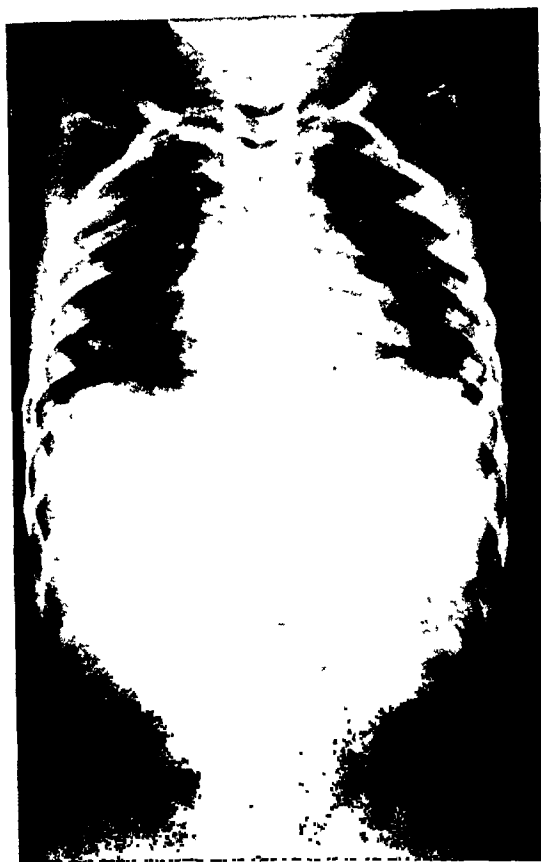


FIG. 7. Eight months postoperative. Normal diaphragm outline and barium-filled stomach in normal position.

borne out by the fact that the two patients in whom the diagnosis was not made until exploration, and where repair was done at a subsequent operation, survived.

We believe the anesthetist should always be prepared to administer a positive pressure anesthesia if the need arises. Many authors stress the importance of this statement. Harrington<sup>4</sup> feels that in the case of a true hernia where a sac is present, the ordinary ethylene or cyclopropane closed anesthesia is satisfactory. However, in the false hernia where no sac is present, it is of great importance to be able to administer positive pressure. The truth of this statement is well verified. (Table VII.)

The higher mortality encountered in the group operated on via the abdominal approach (Table V), would appear to result

at least partially from the fact that more cases were operated on by this method without the benefit of positive pressure anesthesia. Certainly the 7.7 per cent

Most authorities agree that the mortality in children is higher than in adults. The total mortality in this series of sixty-eight cases is 32.4 per cent. A study of the

TABLE V

All Cases			Thoracic			Combined			Abdominal		
No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality	
	No.	Per Cent		No.	Per Cent		No.	Per Cent		No.	Per Cent
68	22	32.4	19	5	26.3	9	1	11.1	40	16	40.0

TABLE VI

When Diagnosed	All Cases			Thoracic			Combined			Abdominal		
	No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality	
		No.	Per Cent		No.	Per Cent		No.	Per Cent		No.	Per Cent
Before operation	63	18	28.6	18	4	22.2	9	1	11.1	36	13	36.1
At operation	5	4	80.0	1	1	100				4	3	75.0

TABLE VII

Anesthesia	All Cases			Thoracic			Combined			Abdominal		
	No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality	
		No.	Per Cent		No.	Per Cent		No.	Per Cent		No.	Per Cent
Positive pressure anesthesia	30	4	13.3	13	3	23.1	6			13	1	7.7
Other types of anesthesia or not recorded	38	18	47.3	6	2	33.3	3	1	33.3	27	15	55.5

mortality in those operated on by the abdominal route, where it is known that a preoperative diagnosis was made, and a proper anesthesia administered, is satisfactory.

mortality with relation to the age of the patient reveals that it is definitely higher during the first year of life. The twenty-four cases under one year of age were all congenital, and the mortality was 50 per

cent. After the first year the mortality dropped to 22.7 per cent. In this group of from 1 to 10 years of age, it will be seen

type. In this table it is seen that by far the most common location is through the left diaphragm. Most of these are false hernias

TABLE VIII

Age of Patient	Entire Series 68 Cases			Congenital and Acquired 54 Cases			Traumatic 14 Cases		
	No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality	
		No.	Per Cent		No.	Per Cent		No.	Per Cent
Under 1 yr.....	24	12	50.0	24	12	50.0	..	..	...
1-10 yrs.....	44	10	22.7	30	9	30.0	14	1	7.1

that in the congenital and acquired cases it is about four times as great as in the traumatic cases.

without sacs. There was one eventration which was operated upon and a repair attempted. This was, however, localized to

TABLE IX

Location	Entire Series 68 Cases			Congenital and Acquired						Traumatic 14 Cases		
				Under 1 Yr. 24 Cases			Over 1 Yr. 30 Cases					
	No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality		No. Cases	Mortality	
		No.	Per Cent		No.	Per Cent		No.	Per Cent		No.	Per Cent
Through left diaphragm	48	15	31.2	20	8	40.0	17	6	35.3	11	1	9.09
Through right dia- phragm.....	1	..	....	..	..	....	1	..	....	..	..	....
Esophageal hiatus—left	11	2	18.2	1	1	100	7	1	14.3	3	..	....
Esophageal hiatus— right.....	3	2	66.7	..	..	....	3	2	66.7	..	..	....
Esophageal hiatus—post mediastinum.....	1	..	....	..	..	....	1	..	....	..	..	....
Eventration left dia- phragm.....	1	1	100	1	1	100	..	..	....	..	..	....
Congenital deficiency or absence left dia- phragm.....	3	2	66.7	2	2	100	1	..	....	..	..	....

Table ix gives the incidence of the location of the hernia, and the percentage mortality with relation to the location and

the central portion of the diaphragm, and could almost be considered as a true hernia. There were also three cases where a

deficiency of the left diaphragm was present. One was described as a complete absence, the other two as deficiencies.

mortality to which organs are displaced into the chest, a study of Table x reveals that there is little relationship between

TABLE X

Viscera Present in Thorax	Entire Series 68 Cases				Traumatic 14 Cases				Congenital and Acquired 54 Cases							
									Under 1 Yr. 24 Cases				Over 1 Yr. 30 Cases			
	Cases		Mortality		Cases		Mortality		Cases		Mortality		Cases		Mortality	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Stomach....	48	70.6	14	29.2	11	16.2	..	....	13	19.1	7	53.8	24	35.3	7	29.1
Colon.....	48	70.6	14	29.2	11	16.2	..	....	18	26.5	7	38.9	19	27.9	7	36.8
Small bowel.	44	64.7	17	38.6	8	11.7	1	12.5	20	29.4	9	45.0	16	23.5	7	43.7
Spleen.....	28	41.2	9	32.1	9	13.2	1	11.1	9	13.2	5	55.5	10	14.7	3	30.0
Omentum...	11	16.2	3	27.3	4	5.9	1	25.0	3	4.4	1	33.3	4	5.9	1	25.0
Left lobe of liver.....	5	7.3	..	....	5	7.3	..	....	..	....	..	....	..	....	..	....
Edge of liver	2	2.9	1	50.0	..	....	..	....	1	1.4	1	100	1	1.5	..	....

Regarding the relationship of the "contents of the hernia" to the mortality, rather one should say, the relationship of the

TABLE XI

Viscera Present in Thorax	No. Cases	Mortality	
		No.	Per Cent
Small bowel without stomach and colon.....	6	5	83.3
Small bowel and stomach	2	1	50.0
Small bowel with stomach and colon.....	26	9	34.6
Colon and stomach.....	8	2	25.0
Colon without small bowel, stomach.....	4	1	25.0
Small bowel and colon...	10	2	20.0
Stomach without small bowel, colon.....	12	2	16.7

Summary of Table

Small bowel with or without other viscera.....	44 (64.7%)	17	38.6
Other viscera without small bowel.....	24 (35.3%)	5	20.8

which viscera are present in the thorax, and the mortality, except in the case of the small bowel. The presence of the small bowel definitely increases the mortality figure. This is more clearly shown in Table xi. If small bowel is present in the thorax, the mortality is nearly twice as great as when it is not present. A study of Table i reveals, however, that the stomach, colon, small intestine, or some combination of the three is present in all of the sixty-eight cases. They seem to be the important organs to consider.

The presence or absence of the spleen, omentum or liver, seems to have little bearing upon the outcome. One might suppose that the presence of the entire left lobe of the liver might produce greater cardiac and pulmonary embarrassment. However, all five of these cases are traumatic, and over 1 year of age, and all lived. This brings up the possibility that the presence of the left lobe of the liver in the left thoracic cavity means that the rent in the diaphragm is large and less likely to

compress the bowel. Also, with the left lobe of the liver in the thorax, there is certainly less room for bowel to protrude into it. We consider the presence or absence of the omentum as unimportant. Some authors have experienced some difficulty with hemorrhage in removing the spleen.

#### CONCLUSIONS

The operation for the repair of the diaphragmatic hernia is still a relatively rare surgical procedure in children. This paper reports and analyzes sixty-eight such cases which have occurred in the course of the past fifty years. The diagnosis of diaphragmatic hernia is more frequently made in the male than in the female, and the operative mortality is higher in the latter. The most common type is the false hernia through the left diaphragm.

A diaphragmatic hernia constitutes a menace to the life of the patient. Early diagnosis is essential. In many cases where the hernia is the cause of death, the diagnosis is not made until the autopsy is performed. A routine post-mortem x-ray in infants and young children in unexplained deaths, might reveal a higher incidence of diaphragmatic hernia than is at present suspected. Due to improved roentgenologic technique, many more cases are diagnosed during life than formerly. More cases have been operated upon during the past eight years than in the previous forty. In many cases in this series, the diagnosis was not made until the x-ray was taken. We therefore believe that we cannot stress too strongly the importance of early roentgenologic studies.

Under 1 year of age, dyspnea, cyanosis, and vomiting are the most frequently listed symptoms, while over 1 year, vomiting, pain, and obstruction occur more often. The mortality is higher during the first year of life. The presence of the small bowel in the thorax, increases the mortality figure, as do signs of a partial or complete obstruction.

A preoperative diagnosis is essential. This allows for proper preparation, first

with regard to the patient's general condition, and second with regard to the preparation for the operation itself. Crushing the phrenic nerve, lavaging the stomach, preparation for the administration of positive pressure anesthesia, are all important.

Except in the case of a symptomless infant under 1 year of age, a definite diagnosis of a diaphragmatic hernia should be followed by a surgical repair at the earliest opportunity.

The following is a case report of a diaphragmatic hernia which was successfully repaired, and which illustrates some of the points brought out in this paper.

#### CASE REPORT

The patient was a white female child of 2½ years, who twenty minutes before admission to the hospital was struck on the left side by a truck. In addition to a fracture of the right humerus, she had many abrasions over the head, abdomen, and left upper thigh. Her condition appeared quite critical, as her blood pressure was 64/30, her pulse was over 160, temperature subnormal, and her respirations labored and rapid. The chest was wrapped in bandages, which provided temporary fixation to the right humerus, and was therefore not examined. The abdomen was soft, but quite tender, especially over the left side. Peristalsis was normal. Owing to the lack of other physical findings in the abdomen, we felt that there was a good possibility that the injury in this area was localized to the abdominal wall.

The child was treated by intravenous injections of 5 per cent glucose, and local heat applications. She gradually recovered from her shock. Her white count was 19,550, hemoglobin 9.6 Gm., and her urine contained an occasional white cell and a moderate number of red cells. By the following morning it was evident, despite persistent voluntary rigidity, that there was little likelihood of a ruptured viscus, and the child was allowed fluids. Her improvement permitted further study, and it was found that there was gas shadows within the left lung field, as seen by x-ray, and a diagnosis was made of herniation of the stomach and much of the bowel through the left diaphragm. The respirations remained rapid and the temperature was persisted elevated from 1 to 3 degrees.



The question arose concerning immediate repair of the hernia, but the child's condition indicated that this would be more dangerous than advantageous. Since there was small bowel present in the hernia, it was thought best that the child be operated as soon as her condition warranted, rather than wait until she was older, because of possibility of intestinal obstruction.

She was placed on multiple small feedings, and by the second week was up and about the ward. Five weeks after the accident, she appeared quite normal, her humerus was united in good position, and her blood picture was normal. The left phrenic nerve was crushed, and produced paralysis of the left hemidiaphragm.

Three weeks later when the child appeared in good condition, repair of the hernia was undertaken. Preoperative preparation consisted of aspiration of the stomach content through a nasal catheter which was left in place, and a transfusion of 200 c.c. of citrated blood. We were fortunate in having available a well trained anesthetist, Dr. Frank Murphy, to whom thanks are due for a well administered positive pressure anesthesia.

A left subcostal incision was made. Exploration revealed the stomach, most of the small intestine, the transverse splenic flexure of the colon, and the upper third of the spleen within the left thoracic cavity. This was withdrawn, and the rent in the diaphragm was picked up with forceps. It was about 7 cm. long. A loop of small intestines (which appeared to be the duodenum) was firmly adherent to the lower flap. This was dissected free. The lower flap of the diaphragm was then sutured to the superior surface of the upper flap 1 inch from the free margin with interrupted mattress sutures of silk. The free margins of the upper flap were then sutured to the inferior surface of the lower flap with interrupted sutures of silk. There was a slight amount of oozing from the area just above the pancreas, and this was controlled with a single iodoform pack.

The patient stood the operation well. On her return to the ward she was quite cyanotic, and was placed in an oxygen tent. The pulse was 130 to 150, the respirations 30 to 50, and the temperature as high as 102 degrees. A second 250 c.c. transfusion was given later in the day, supplemented by 200 c.c. of saline. Carbon dioxide and oxygen inhalations were given every three hours. On the following day her

condition remained about the same. So much difficulty was encountered in the administration of intravenous fluid, that hypodermoclysis was begun. She was also given 100 c.c. retention enemas of warm tap water every four hours. On the following day, as the patient refused fluids, a nasal catheter was inserted, and water, 1 to 2 ounces every hour, was introduced into the stomach through the tube, and she was given hard candy to suck. On the next day a formula was made up and injected through the tube. A portable x-ray showed 70 per cent collapse. We considered aspirating some of the air from the left thorax, but she seemed to be doing so well, that it was thought best to leave her alone. The pack was removed on the fourth day. By the fifth day the patient was taking nearly 1,000 c.c. of fluid by mouth, and the nasal catheter was removed. From then on her convalescence was uneventful. X-rays showed gradual expansion of the left lung.

Within two weeks from the date of operation she was able to be out of bed. She was last seen ten months after the operation, at which time she appeared quite normal and healthy.

#### REFERENCES

1. HEDBLUM, C. A. Diaphragmatic hernia. In Lewis' Practice of Surgery, 5: 1-66, 1937.
2. HEDBLUM, C. A. Diaphragmatic hernia. *Ann. Int. Med.*, 8: 156-169 (Aug.) 1934.
3. RANKIN, F., and GRIMES, A. Diaphragmatic hernia. *Kentucky M. J.*, 35: 281-286 (June) 1937.
4. HARRINGTON, S. W., and KIRKLIN, B. R. Clinical and roentgenologic manifestations and surgical treatment of diaphragmatic hernia with a review of 131 cases. *Radiology*, 30: 147-156 (Feb.) 1938.
5. TRUESDALE, P. E. Diaphragmatic hernia in children with a report of thirteen operative cases. *New England J. Med.*, 213: 1159-1171, 1935.
6. ORR, T., and NEFF, F. C. Diaphragmatic hernia in infants under one year of age treated by operation. *J. Thoracic Surg.*, 5: 434-439 (April) 1936.
7. LISSOWETZKY, V. Congenital diaphragmatic hernia in the newborn. *Zentralbl. f. Gynäk.*, 59: 276-284 (Feb. 2) 1935.
8. GREENWALD, H. M., and STEINER, M. Diaphragmatic hernia in infancy and in childhood. *Am. J. Dis. Child.*, 38: 361-392 (Feb. 1) 1929.
9. WOOLSEY, J. H. Diaphragmatic hernia. Section on Surgery, General and Abdominal, A. M. A., pp. 204-229, 1927.
10. O'DWYER, J. Diaphragmatic hernia with operation. *Arch. Pediat.*, 6: 882-886, 1889.
11. MAYLARD, A. A case of strangulated hernia. *Glasgow M. J.*, 46: 143-146 (Aug.) 1896.
12. AUE, O. Congenital diaphragmatic hernia. *Deutsche Ztschr. f. Chir.*, 160: 14-35 (Nov.) 1920.
13. MCCLEAVE, T. C. A case of diaphragmatic hernia. *Am. J. Dis. Child.*, 13: 252-255, 1917.

14. DOWNES, W. A. Congenital hernia of the diaphragm. *Surg., Gynec. & Obst.*, 27: 393-397 (Oct.) 1918.
15. DEBUYS, L. R. Anomaly of diaphragm with herniation into the thorax of certain viscera. *Am. J. Dis. Child.*, 19: 55-61 (Jan.) 1920.
16. GREIWE, J. E. Report of a case of diaphragmatic hernia. *Arch. Pediat.*, 37: 593-599, 1920.
17. SPEIK, F. A. Discussion of diaphragmatic hernia diagnosed during life by Milton M. and Sidney A. Portis. *J. A. M. A.*, 75: 1264 (Nov. 6) 1920.
18. TRUESDALE, P. E. Symptoms and physical signs indicating hernia of the diaphragm with report of twelve cases treated by operation. *Ann. Surg.*, 94: 528-538 (Oct.) 1931.
19. TRUESDALE, P. E. Diaphragmatic hernia; the thoracic approach. *Tr. Am. S. A.*, 300-314 (Sept.) 1921.
20. GOETSCH, EMIL. Personal communication.
21. GORDON, M. B., and GOLANN, D. L. Traumatic diaphragmatic hernia in a girl of eight years. *Am. J. Dis. Child.*, 22: 579-585 (Dec.) 1921.
22. BARNETT, G. S. Congenital deficiency of the diaphragm. *Brit. M. J.*, 1: 602 (April) 1921.
23. LEPOUTRE. Case of congenital diaphragmatic hernia in a three months' old infant. *Bull. et mem. Soc. de chir. de Paris*, 48: 170-177, 1922.
24. BEHREND, M. Diaphragmatic hernia in a child. *Arch. Pediat.*, 41: 408-412 (June) 1924.
25. CARMAN, R. D. and FINEMAN, S. The roentgenologic diagnosis of diaphragmatic hernia with the report of 17 cases. *Radiology*, 3: 26-45 (July) 1924.
26. SHERWOOD, W. A. Case report. *Ann. Surg.*, 81: 1026-1028, 1925.
27. JOWERS, R. F. A case of diaphragmatic hernia. *Brit. J. Surg.*, 15: 332-333 (Oct.) 1927.
28. SHACKLETON, W. E. Traumatic rupture of the diaphragm. Personal communication. *Surg., Gynec. & Obst.*, 44: 684-686 (May) 1927.
29. STEPHENS, H. D. Diaphragmatic hernia in children. *Australian & New Zealand J. Surg.*, 5: 161-169 (Oct.) 1935.
30. CLARK, D. F. Diaphragmatic hernia including report of cases with x-ray films. *Illinois M. J.*, 52: 63-68 (July) 1927.
31. TOREK, F. Discussion of diaphragmatic hernia by S. W. Harrington. *Arch. Surg.*, 16: 386-415 (Jan.) 1928.
32. LEOPOLD, J. S. Non-traumatic diaphragmatic hernia; report of a case in child aged 4 years. *Am. J. Dis. Child.*, 33: 597-601 (April) 1927.
33. PAUCHET, V. and LUQUET, G. Diaphragmatic hernia of the stomach; case. *Bull. Acad. de méd. Paris*, 99: 92-96 (Jan.) 1928.
34. OLMSTEAD, H. C. Non-traumatic lesions of the diaphragm in infancy and childhood. *Northwest Med.*, 27: 169-176 (April) 1928.
35. MEYER, W. Discussion of diaphragmatic hernia by S. W. Harrington. *Arch. Surg.*, 16: 386-415 (Jan.) 1928.
36. BETTMAN, R. B., and HESS, J. H. Incarcerated diaphragmatic hernia in an infant with operation and recovery. *J. A. M. A.*, 92: 2014-2016 (June) 1929.
37. MCFADDEN, G. D. E. Congenital diaphragmatic hernia. *Brit. M. J.*, 2: 45-46 (July 13) 1929.
38. BROWN, H. P. Diaphragmatic hernia. *S. Clin. North America*, 9: 1191-1194 (Oct.) 1929.
39. SANDERS, R. L. Diaphragmatic hernia. *Ann. Surg.*, 91: 367-380 (March) 1930.
40. SCHONBAUER, L., and WARKANY, J. Successful surgical treatment of congenital diaphragmatic hernia in nursing; case. *Ztschr. f. Kinderheilk.*, 50: 125-131, 1930.
41. HARRINGTON, S. W. Diaphragmatic hernia associated with traumatic gastric erosion and ulcer. *Surg., Gynec. & Obst.*, 51: 504-521 (Oct.) 1930.
42. DONOVAN, E. J. Repair of a diaphragmatic hernia in an infant of four months. *S. Clin. North America*, 11: 521-525 (June) 1931.
43. BETTMAN, R. B., and HESS, J. H. Diaphragmatic hernia in an infant. *Ann. Surg.*, 93: 1274-1278 (June) 1931.
44. EGGERS, CARL. Hernia or eventration of the diaphragm; report of case. *J. Thoracic Surg.*, 1: 41-49 (Oct.) 1931.
45. ROBB, E. F. Congenital diaphragmatic hernia. A report of a successful operation at seven weeks of age. *Journal-Lancet*, 51: 597-600 (Oct. 1) 1931.
46. CORYLLOS, P. N. Two cases of diaphragmatic hernia. *S. Clin. North America*, 14: 285-299 (April) 1934.
47. HIPSLEY, P. L. Congenital diaphragmatic hernia in a young girl. *M. J. Australia*, 1: 200 (Feb. 14) 1931.
48. UNSHELM, E. Hernia hiatus esophageal beim Kinde. *Monatschr. f. Kinderh.*, 51: 94-105, 1931.
49. JOHNSON, H., and BOWER, A. G. Strangulated diaphragmatic hernia in infant. *California & West. Med.*, 36: 48-49 (Jan.) 1932.
50. IIZUKA, L., and SANO, U. Angeborene Zwerchfellhernie beim Säugling. *Orient J. Dis. Inf.*, 11: 23-32 (March) 1932.
51. LAUENSTEIN, H. The symptomatology and diagnosis of diaphragmatic hernia in the infantile period and childhood. *Zentralbl. f. d. ges. Kinderh.*, 54: 117, 1932.
52. BRYCE, A. G., and GRAY, E. D. Unusual difficulties in diagnosis of hernia (presence of spleen in sac). *Brit. J. Surg.*, 20: 692-694 (April) 1933.
53. PIERRET, RENÉ, and BRETON, A. A case of right diaphragmatic hernia containing a loop of colon in a child seven years old. *Echo med. du Nord*, 1: 430-444 (March) 1934.
54. BARRETT, N., and WHEATON, C. Pathology, diagnosis and treatment of congenital diaphragmatic hernia in infants. *Brit. J. Surg.*, 21: 420-433 (Jan.) 1933.
55. WEINBERG, J., and HAMILTON, H. Congenital diaphragmatic hernia in an infant with successful operation. *Nebraska State M. J.*, 20: 241-244 (July) 1935.
56. MIMPRISS, T. W. A case of diaphragmatic hernia. *Brit. J. Surg.*, 24: 619-622 (Jan.) 1937.
57. DONOVAN, E. J. Personal communication.
58. BIRD, E. Division of ribs as an aid in closing diaphragmatic hernia. *Ann. Surg.*, 104: 993-1011 (Dec.) 1936.
59. STOBIE, G. H. Diaphragmatic hernia; a review of recent literature and a report of 5 cases. *Canad.*

- M. A. J., 36: 136-141 (Feb.) 1937. Personal communication.
60. HARRINGTON, S. W. Personal communication.
  61. LEWALD, L. T. Congenital absence of the left half of the diaphragm. *Arch. Surg.*, 14: 332-344 (Jan.) 1927.
  62. BECKMAN, E. H. Diaphragmatic hernia. *Surg., Gynec. & Obst.*, 9: 154-156, 1909.
  63. HUME, J. B. Congenital diaphragmatic hernia. *Brit. J. Surg.*, 10: 207-215 (Oct.) 1922.
  64. CLOPTON, M. B. Eventration of the diaphragm. *Ann. Surg.*, 78: 154-163 (Aug.) 1923.
  65. REISS, F. Hernia diaphragmatica congenita bei einem 3-jährigen Kinde. *Jahrb. f. Kinderb.*, 77: 550-559, 1913.
  66. GIUSTINIAN, V., and ANTONELLI, A. Diaphragmatic hernia in infant. *Semana med.*, 1: 314 (Feb. 3) 1927.
  67. BRUSH, J. M. Complete false congenital diaphragmatic hernia. Report of case. *Arch. Pediat.*, 44: 612-619 (Oct.) 1927.
  68. DE LA VEGA, J. C. Congenital diaphragmatic hernia. *Semana med.*, 1: 548-550 (March 1) 1928.
  69. HARRINGTON, S. W. Diaphragmatic hernia. *Arch. Surg.*, 16: 386-415 (Jan.) 1928.
  70. MAYO, C. H. Repair of hernia of the diaphragm. *Ann. Surg.*, 86: 481-484 (Oct.) 1927.
  71. CARRINGTON, G. L. Diaphragmatic hernia; repair of two-stage operation employing preliminary thoracoplasty. *Ann. Surg.*, 89: 512-520 (April) 1929.
  72. HARRINGTON, S. W. Diaphragmatic hernia; symptoms and surgical treatment of 60 cases. *J. A. M. A.*, 101: 987-994 (June) 1933.



. . . THE treatment of choice in cases of acute massive hemothorax is immediate aspiration of the hemothorax followed by injection of air. Where there is a moderate amount of blood in the pleural cavity, recovery will follow expectant treatment or aspiration and air replacement, but the latter treatment shortens the convalescence.

# PITFALLS OF PHRENIC NERVE CRUSHING

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IT seems puerile to discuss so simple an operation as phrenic nerve crushing.

However, like many other simple procedures, its potential complications are so great that they should be frequently emphasized. There is no thoracic surgeon who has not at one time or another been quite taken aback and embarrassed by dallying a considerable time on a phrenic crushing which he had expected to complete in a few minutes. Very often the difficulties are self-made—the outcome of an error of omission or commission in the technical procedure, resulting in the destruction of essential landmarks or in the creation of false ones which eventually lead to major trouble.

As a rule, a 1 or 1½ inch transverse incision, about 1 inch above the clavicle just over the posterior border of the sternomastoid muscle will give a sufficient exposure to identify and crush the phrenic nerve. Care in identifying and preserving the landmarks is essential to a successful operation.

The posterior border of the sternomastoid is easily recognized by palpation upon having the patient raise and turn his head slowly from side to side.

The incision is carried through the platysma and the border of the sternomastoid is then retracted medially, exposing the cervical fascia which covers a pad of fat immediately overlying the scalenus anticus. The fascia should be incised transversely across the muscle and the fat then bluntly separated with a hemostat in the direction of the muscular fibers in order not to disturb the relationship of the nerve to the muscle. This fat layer is very vascular and care should be taken not to tear any vessels and obstruct the field. The nerve is generally seen just lateral to

the medial border of the scalenus anticus, running obliquely downward. If this fails to expose the nerve, blunt dissection should be carried upward to the omohyoid muscle crossing. The scalenus muscle is palpated as a stout band and not infrequently the phrenic can be felt coursing along it immediately behind the omohyoid.

The phrenic, which varies in size, is generally easily identified by the pain felt in the shoulder and neck when it is squeezed with a forceps, although this does not always apply because the nerve is sometimes anesthetized or because the pain is produced only upon crushing. Crushing the nerve at one point with a toothless clamp usually suffices to paralyze the diaphragm for four to six months.

The incision is closed with skin clips or silk sutures which are removed in twenty-four hours to insure a good cosmetic result.

When performed as described, the operation takes ten to twenty minutes. Pitfalls may prolong the operation indefinitely, sometimes render it impossible, and occasionally lead to dire complications.

One of the most common difficulties is brought about by the retraction of the nerve with the cervical fascia and fat pad with the retractors. A fruitless search ensues which opens the door to confusion and danger. The sympathetic nerve, which generally lies behind the jugular vein medial to the scalenus, is mistaken for the phrenic and crushed. The result is a Horner's syndrome which lasts for months and sometimes is permanent. On occasion this may lead to an ulcer of the cornea.

The carotid sheath may unintentionally be opened, the vagus exposed and deliberately or inadvertently crushed, producing a paralysis of the muscles supplied by the recurrent laryngeal nerve and an

increase in the cardiac rate. The recurrent laryngeal itself has been injured with consequent hoarseness of several months' duration. In one case that has come to our attention (a doctor), it lasted for eight months. This was accompanied by a dryness of the throat which was very harassing to the patient.

The brachial plexus, which is often an important landmark for the lateral border of the scalenus anterior, is not infrequently traumatized, producing considerable disability and pain in the arm.

The long thoracic nerve, which bears a similar relationship to the scalenus medius that the phrenic does to the anticus, has been confused with it because the medius was taken for the anticus.

The brachial plexus proper is not often mistaken for the phrenic because it is much larger, but the subclavian branch which runs parallel to the phrenic on the lateral border of the scalenus anticus is frequently crushed instead of the phrenic. However, injury to the brachial plexus resulting from this operation has been reported several times, probably due to pressure from retraction.

Hemorrhages of considerable severity occur from injury to the jugular and subclavian veins and thyroid axis. Some of these have required ligation of the jugular or subclavian veins and artery and three deaths from uncontrollable bleeding are reported.

When hemorrhage of any magnitude occurs, it is best not to attempt to grasp the blood vessel through so small an incision. The bleeding should be controlled by a tight tampon and pressure exerted by an assistant while the incision is enlarged and adequate exposure is

obtained. Otherwise greater damage may be done by blind attempts at clamping vessels.

It is generally in such a situation or in a field obscured by blood that the pleura is punctured or torn, producing a pneumothorax and sometimes mediastinal emphysema.

Lacerations of the jugular and subclavian veins have resulted in four deaths from air emboli, according to reports found in foreign and American literature.

The thoracic duct is not infrequently injured; this is recognized by an immediate or subsequent escape of chyle. It can generally be controlled by the application of a snug tampon although in some instances the duct has to be ligated. In twenty cases of this accident, one death occurred three weeks after operation.

With due care, meticulous attention to minute details and orderly dissection of well defined landmarks, none of these complications should occur.

#### CONCLUSIONS

The technique and procedure for exposing the phrenic nerve are outlined and the numerous pitfalls that may convert this simple and minor operation into a complicated, serious and even fatal procedure are emphasized. The reasons for and the means of avoiding the errors which lead to difficulties and disaster are set forth and discussed.

A phrenic nerve crushing remains simple and safe only if each step of the operation is clearly borne in mind and the anatomic landmarks are well preserved. A large incision which leaves an unsightly scar is not necessary for adequate exposure of the phrenic nerve.



# THE ROLE OF THE THYROID IN GASTROINTESTINAL DYSFUNCTION

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**D**URING periods of unusual economic and political adjustment there is often a coincidental increase or decrease in the number of certain types of gastrointestinal dysfunction which present themselves for diagnosis, paralleling heights and depths of crises.

This has been so consistent that it was felt that if studied comparisons were to be made, it would be found that the period during which the largest percentage of these cases was met with would parallel the low points of the Dow-Jones' averages or the low points of the various indices of business activity, and correspondingly that fewer of these cases were seen when these same indices reached high levels.

In the observation and study of such a group of cases, one is surprised to find that in only a very small percentage is true organic pathology found, and when found it is most often a duodenal ulcer.

Male patients predominate in this series of cases as they would in any similar group, although it is very possible that females, subjected to the same economic and environmental influences could form a large percentage. There is a smaller group of females, numerically speaking, comprised of wives who are conversant with their husband's business affairs, and who share intimately the economic pressure, worry, fear and apprehension and conversely the freedom from such, who enter into such a series of cases.

Analysis of the personal characteristics of the male patients demonstrates that they are predominantly of one type: the high pressure, hard driving business man, carrying an unusual load of responsibility—brokers, bond traders, speculators, the heads of larger organizations.

Crile described this particular type of individual in his treatise on hyperkinesia, calling them "hyperkinetics." He made a detailed study of the type, endeavoring to prove that they are the objects of a tremendous continuous adrenal drive, which eventually fatigues and wears itself out over a period of time. It is intriguing to speculate as to whether all business men of the hyperkinetic classification are possessed of this hyperadrenal drive as a part of their natural body makeup, or whether the acceptance of unusual business responsibility forces this drive.

In a study of such a group of cases it became necessary to ascertain the reason for the symptoms complained, ruling out, insofar as possible, the existence of any definite organic pathology.

Everyone, medically speaking, is familiar with Cannon's researches on the effect of the emotions upon the physiology of the gastrointestinal tract, particularly with regard to changes in motility and secretion, under such environmental states as worry, fear, anger, love, and hate. Determination of the "modus operandi" of these deviations from the normal physiology was necessary in order better to understand and correct the dysfunction.

Before going into the details of such a study, it would be in order to enumerate the symptoms usually complained of by these patients. They can be divided into three distinct groups, if classified according to localization of symptoms:

*Group I.* In which symptoms are cervical and substernal in location:

1. A substernal pressure and discomfort, usually high under the manubrium, rarely described as a pain, more often as a feeling

that something feels definitely wrong in this area.

2. "Globus hystericus"—a feeling of a lump or ball in the throat which incites constantly repeated swallowing in a more or less unsuccessful attempt to get rid of the sensation.

3. Aerophagia—a continuous swallowing of air and production of gaseous belching in an effort to produce one single satisfactory voluminous elimination of gas, giving momentary relief only, the process being immediately reproduced, so that a vicious circle is established and constant repetition takes place.

4. A sensation high in the left upper quadrant of the abdomen as of a constriction hindering the passage of food; small amounts of food seem to lodge here and not pass on; much the syndrome a patient with true cardiospasm would complain of except that the localization of symptoms is slightly lower.

*Group II.* In which symptoms are predominantly gastric or gastroduodenal in type:

1. A feeling of tension, of constriction, but not of actual pain in the midepigastrum.

2. Heaviness and uneasiness in the midepigastrum after a very small amount of food intake, so that the patient does not feel like eating more, although often hungry.

3. Mild nausea with resort to voluntary induction of vomiting to produce temporary relief of symptoms, then the cycle repeating itself.

4. Borborygmus and mild upper abdominal cramping pains, colicky in nature.

5. Ease and relief from symptoms if stomach is empty so that many patients are undergoing what amounts to an involuntary fasting, in order to procure freedom from distress.

6. General asthenia, loss of weight, insomnia, nervous and emotional instability. The latter subjective states are usually quite pronounced.

*Group III.* In which symptoms are localized in the lower abdomen and pertain to the colon.

1. Minor generalized low abdominal soreness and tenderness without spasm; shifting, cramping, colicky type of pain, mild in degree.

2. Marked intestinal flatulency with an inability to expel gas for relief.

3. A distinct change in bowel function which may be from a constipation to a series of unsatisfactory, frequent, chopped up type of movements, or the change may be from fairly normal bowel function to obstinate constipation.

4. Mental sluggishness, slow cerebration, loss of memory, headaches, dizziness, and tinnitus are quite common.

5. Insomnia, due to an inability to relax and to avoid mental concentration upon the problems in hand. In some case the low abdominal discomfort occurs most often in the early hours of the morning, interrupting and cutting short the number of hours of obtained sleep.

Such a classification summarizes all too briefly the three principal groups into which these patients may be classified from the standpoint of localization of symptoms only. It would be possible to add minor groups, occurring less frequently and consisting of those cases in which a combination or combinations of any of these three existed. Less commonly encountered is yet another group, in which detailed history taking reveals the fact that symptoms occur only during the day when the dynamic drive is on, passing off at night after the day's physical let-down, when relaxation takes place. These groups would be found rather small in actual number, and their inclusion in the main classification only obscures the issue.

Adequately to aid a group of such patients, it is necessary to peer behind the scenes, so as to speak, to get beneath the surface, and attempt a visualization of the acting mechanical forces which are interfering with normal physiology and producing the abnormal, and to ascertain in

what manner these forces are acting to accomplish this.

It is obvious that a comprehensive detailed discussion of these factors could not possibly be within the scope of a paper. For that reason only the highlights will be touched upon and these but briefly.

There exists in the body the endocrine group of glandular structures composed of the thyroid, the pituitary, the adrenal and ovary, and other less important ductless gland structures, acting either singly or in combination to produce certain definite chemical substances which we call hormones. These substances or hormones are transferred directly into the blood stream, there to perform the specific function for which they have been designated by specialization. It is vitally necessary that all of these substances shall be in certain definite ratio not only to the system as a whole, but also to one another. This is specifically true because some of these substances act synergistically. Any deviation, therefore, from the normal equilibrium in the amounts present in the blood stream or produced by the glands themselves brings about a definite change from the normal physiology.

The changes away from the normal physiology are often brought about through the action or lack of action of these hormonal substances upon the autonomic nervous system. It is by way of this complex system of nerve structure that the actual changes from the normal are brought about.

Eppinger, of Vienna, some years ago first introduced the concept of the synergistic action of the two parts of the autonomic nervous system, the sympathetic and the parasympathetic, maintaining that they must be kept in more or less constant equilibrium, and designating the deviations from this normal equilibrium as vagotonia and sympatheticotonia.

In this particular group of cases, rather consistently there is found a disturbance in the patient's emotional state, such as that produced by a sudden mental shock, by a prolonged period of worry and anxiety, or

the presence of a sense of fear, sudden or continued, over a period of time, of possible impending disaster or catastrophe. This latter is usually economic and related to business. Anger or frustration, usually in the realm of love or of money, will be present in others, often with an inadaptability to reality, producing a subjective resentment and an extreme degree of emotional imbalance. These underlying emotional states are admittedly purely psychic, but the mind, influencing the entire body by way of the autonomic system, produces changes in the productive pace of the thyroid, the pituitary, the adrenal or the ovary with a resultant hormonal imbalance in body equilibrium so essential to normal physiologic function. This imbalance is specifically in the amount of hormonal production, the increase or decrease acting by way of the autonomic nervous system to produce changes in action and function of smooth muscle fiber and secretory gland activity, such as spastic contraction or atonic dilatation, with attendant stimulation or inhibition of function.

The actual mechanics involved are similar in all of the groups of cases. The anatomic site of initiation of symptoms differs in each group. Stimulation of the vagus, we know, causes spastic contraction of smooth muscle fibers. Thyroid extract fed into the blood stream in variable amounts, differing according to each individual, will cause exactly the same type of contraction. Disordered psychic states can stimulate both the vagus and the thyroid, directly or indirectly, causing temporary or intermittent over-dosages of thyroid extract, most often not sufficiently continuous as to produce a true hyperthyroidism, but sufficient to incite the syndrome of intermittent or continued pharyngeal, cardiac, and pyloric spasm, because of the contractive action of the smooth muscle in these areas. There exist two additional factors of importance: first, the majority of these patients, in order to provide themselves with an escape



mechanism, or a sort of psychic prop or crutch, take refuge in excess alcohol intake or tobacco smoking. Both of these, being definite toxic irritants to the sympathetic nervous system, thereby serve to complicate and add to the instigating or inciting factors. Secondly, women, mainly, have sought this same escape in hypnotics and sedatives, used in ever increasing dosage, a factor certainly not conducive to sympathetic system equilibrium.

Evidence has been discovered and corroborated in the experimental laboratory, that certain definite chemical substances derived from the end products of protein metabolism are liberated at the very periphery of the tiny nerve fibrils comprising the sympathetic nerve system and that these chemical substances are absorbed by the cell structures immediately adjacent, through the cell membrane into the cytoplasm, by means of an osmosis-like process, thereby influencing the function of those individual cells. The chemical product so liberated is influenced both as to amount and actual chemical composition by the state of equilibrium of the ductless gland system which, in turn, is influenced by just such disturbed states of emotion as outlined above.

A specific example of a substance so liberated is acetylcholine, which in proper amount maintains the individual body cell in protoplasmic balance, in over-amount causes dilatation and increased water retention of the individual cell. The far-reaching effects of large doses of acetylcholine on large members or groups of cells need not be gone into. Another illustrative example is the liberation into the liver and the intestine of an adrenalin-like substance termed sympathin, created by sympathetic stimulation. The effects of large doses of this product on large numbers of the smooth muscle fibers of the intestine are easily visualized. The same holds true of the liver, excessive dosage impairing normal function.

It is not to be assumed that emotional states or disturbances influence thyroid

action alone. They have a direct influence upon the parathyroids, therefore indirectly upon calcium metabolism and permeability of cell membrane, upon the adrenals, therefore upon blood pressure and smooth muscle tone of vessels and capillaries, upon the ovaries, therefore upon body metabolism, thermic regulation and stability. It must be borne in mind, however, that any and every disturbance of the thyroid, regardless of how minor, does mean disturbance in the function of these other structures, or a polyglandular disarrangement. Such disturbance can be confined only to one gland, but more often secondary features are present, causing disturbances in other structures.

The immense ramification of the endocrine system and of the sympathetic is of exceptional complexity. The thyroid, however, seems to play the more outstanding rôle in all the disturbed changes which take place, and more so in the types of cases mentioned herein.

The part played by it in protein digestion, influencing the oxidation of the amino acids into urea, thereby influencing the urea content of the blood, is of no minor importance. It acts synergistically with the adrenal, influencing both proteid and carbohydrate digestion by way of sympathetic fibers to the pancreas. It has a direct influence upon the parathyroid, influencing thereby calcium balance. Its direct influence upon the pituitary regulates to a certain extent the water balance of the body. One could go on enumerating its multiple ramifications and secondary functions but space does not permit.

Disturbance of thyroid rhythm and pace, and secondarily of autonomic equilibrium, result in changes in blood hormone content, thereby affecting proteid and carbohydrate digestion. The chemical end products of such digestion are thus disturbed, both as to quantity and composition, producing changes in smooth muscle function and secretory gland activity. Specifically, they produce the pharyngeal and esophageal spasm, encountered in the cases in Group I.

The same disturbed mechanism accounts for the high substernal pressure and discomfort, the spasm of the pharyngeal and upper esophageal musculature, acting through or by way of the cervical sympathetic, to produce the "globus hystericus" and the aerophagia complained of by the patients in this group.

As to the mechanics of symptom production in the second group of cases—the musculature of the stomach being composed entirely of smooth muscle, is regulated and coördinated by the autonomic nervous system. Gastric secretion is controlled also by the autonomic, but the specific parts played by the sympathetic and parasympathetic portions is not definitely understood. It is presumed that the sympathetic exerts its action upon the chief and parietal cells of the glands of the fundus to excite the secretion of hydrochloric acid, while the parasympathetic controls the water secretion of the stomach, thereby controlling the degree of concentration of hydrochloric acid, depending upon how little or how much water is added to it.

With sympathetic irritation there is a tendency for dilatation of smooth muscle, so that an atonic, dilated stomach with a wide open patent pylorus is encountered, food passing almost immediately from the stomach into the intestine, which is ill-fitted physiologically to carry on the first stages of digestion. With sympathetic stimulation the adrenal influence upon the pancreas is also affected so that a resultant depression of pancreatic function takes place, serving to aggravate the problem of food digestion by impairment of the rôle played by the upper part of the small intestine.

Alvarez recently pointed out that in impairment of digestive function the small intestine had a great share, particularly with reference to the production of gastric symptoms.

The opposite picture from that produced by sympathetic irritation can also take place in the stomach: spasm or contraction

of the smooth muscle, most often in the region of the pylorus, due to stimulation of the parasympathetic. Which one of the two systems, sympathetic or parasympathetic, obtains the ascendancy in control may vary, depending entirely upon the physico-biologic makeup of the individual, and the influence of his environmental and emotional state. Both may be irritated simultaneously, producing even greater disturbance in equilibrium, greater imbalance, greater disorganization.

With a contracted spastic stomach musculature and a pylorospasm, the syndrome of feeling full and distressed after a small amount of food intake is accounted for, as is also the duodenal type of symptom syndrome encountered in this Group II of cases.

The mechanism involved in production of symptoms in Group III is identical except that a lower anatomic division of the autonomic is involved, exerting its influence upon a lower anatomic segment of the gastrointestinal tract.

The site of action of these sympathetic impulses depends upon whether they originate in or about the cervical, celiac or splanchnic plexi, or lower still in the superior or inferior mesenteric or hypogastric plexi.

The intimate relationship between the emotions and the gastrointestinal function has long been an established clinical fact. Everyone knows from personal experience that agreeable, pleasurable emotions are conducive to a better state of digestion and intestinal function and that disagreeable emotions produce the contrary. Pavlov, Cannon, and Ivy have described instances of complete inhibition of gastrointestinal motility and of glandular secreting activity as the result of emotion. In more recent years these same men have been confirming how and by what actual physical means these changes take place.

Usually the gastrointestinal reaction to an emotion exists only for as long as the original incitor persists, subsiding when the emotion ceases or changes. The indi-

vidual possessed of a stable, well developed nervous system kept under control, is able in a large measure to throw off or suppress any expression of emotion. His visceral response to emotion may be intense, but only momentary, returning immediately to normal physiologic balance. An unstable individual, or one who has been made so by long continued conflict with emotions, particularly if this conflict is unsuccessful, does not snap back to the physiologic normal so quickly; there is either a time delay in his reversal or no return at all to the normal.

The first individual possesses what we choose to call "physiologic adaptation." Even in such an individual, however, continued irritation by a disagreeable emotion over a period of time can affect his power of adjustment, the time interval required for snapping back to normal becoming increasingly prolonged up to a hypothetical point of complete exhaustion of this power.

The more frequent and more severe the emotional upset, the more the ability of the individual to "take it" becomes impaired. The next time it will make a greater impression upon him, and each time his resistance to it is lessened, because the underlying factors, the thyroid, adrenal, pituitary, carrying the load, become impaired in their capacity to respond, through sheer fatigue from overwork.

It is in such manner that the symptoms of these three groups of cases have been brought about by:

*First:* Impaired physiologic response to emotional stimuli.

*Second:* Disorganization of the equilibrium of the autonomic nervous system, the sympathetic or the parasympathetic being in command, depending upon the physcobiologic makeup of the individual, influenced by his environmental and emotional state.

*Third:* Direct action upon the endocrine system, mainly through the thyroid and adrenal.

*Fourth:* Deviation from the normal in the function of the smooth muscle structure and the glandular secreting activity of the stomach and pancreas takes place, producing the symptom syndromes complained of, depending upon which anatomic group of sympathetic plexi impulses originate at.

#### DISCUSSION

Considerable confusion and lack of recognition exists as to these groups of patients. Of prime importance is to rule out, by means of intensive search, any organic pathology. It must be kept constantly in mind that the possibility exists of the supposedly functional being so prominent as to mask the existence of an actual organic lesion.

Because of the psychic makeup of the individuals composing these groups there exist exceptional opportunities for introspection and self-analysis, which are, more often than not, detrimental to the individual. This introspection can be of such degree as to cause a disorganization of the personality and even a psychosis. One must differentiate this group and not confuse it with the groups outlined here. These cases are more in the realm of psychopathology. In some few of these latter, laboratory procedures may be of help in differentiation. Willful invalidism, malingering, symptoms of an escape mechanism from daily problems, serve only to test the physician's observation and diagnostic acumen.

It will be found in these groups that very often there exist associated ailments not directly referable to the chief complaint, but indicative rather of the low state of body metabolism and resistance, for example, an associated sinusitis, neuritis, arthritis, migraine, or phlebitis.

Objective and laboratory procedures may be of some help or none at all.

Blood pressure readings are important in discovering a true hypotension or a clue to a true adrenal insufficiency.

Complete blood examination, including cell count and differential, may uncover an underlying secondary or primary anemia

which would have to be corrected in the course of bringing the patient to normal equilibrium.

Basal metabolic determination is important, as a large group of these individuals tend toward a hypothyroid state. When one is faced with distinguishing between true hypothyroidism, a blood cholesterol determination is of value, invariably being raised in the true hypothyroid.

Gastric analysis will in some cases reveal a low concentration of free HCl or even a definite achylia, in others the exact opposite. The mechanism of HCl production and its deviations in these cases has been discussed.

Roentgenologic examination of the gastrointestinal tract, more particularly fluoroscopic examination, will reveal the state of muscle tone of the stomach itself, the patency or spasticity of the pyloric sphincter, the degree of intensity and frequency of peristaltic activity present, and much additional information of value.

Some of these cases present certain aspects of hyperthyroid activity, others of hypothyroid, others of a hypoadrenalin function. Each such type must be differentiated in order to institute successful therapy. Pavlov's conception of life is most adaptable in explanation of this group of cases, because they represent those who temporarily are disintegrated. He maintained that man in his normal state represented a beautifully integrated, harmoniously acting, complex mechanism, indicating physiologic equilibrium. Brown-Sequard gave to this idealistic state a term, "*Le milieu interieur*"—or that state of the body when all of the hormones, all of the electrolytic ions, the vitamins, the enzymes and the products of anabolism and catabolism exist in their proper proportion and proper relationship.

How complex this thing we call life is. As medical men we all are concerned with deviations from this ideal state, and with the restoration of the individual to the closest possible approach to this state. It is with such a thought in mind that attention

is called to this group of cases that they may be the recipients of more studious and intelligent effort, and not be classed indiscriminately as neurotics.

#### THERAPY

It is obvious that to treat visceral manifestation of emotional and environmental stress without attempting to remove the cause would be futile. Therefore in therapy must be considered an abrupt severance of proximal influence.

*Environmental Change.* For various reasons environmental change is most desirable. It immediately removes the individual from the source of his irritation. Distance tends to diminish the intensity of situations. What seemed unsurmountable and mountainous because of its very propinquity does not seem so terrifying from farther away. Sober evaluation takes place, fear and uneasiness diminish or are banished completely.

*Psychotherapy.* The therapeutics of the mind offers an opportunity for the institution of measures tending to restore functional balance and normal emotional equilibrium. The physician by a rational explanation of the actual physical factors involved in the production of symptoms may be able to banish apprehension and fear on the part of the patient. Better coöperation results and a faster return to normal. This is the more easily applicable to the patient possessed of a sufficiently understanding intelligence.

Instruction may provide an adaptation to problems, psychic adjustment, may aid the disciplining of the emotions. Patients fear that which they do not know; given a rational explanation, fear is banished and the first step in the restorative comeback produced.

*Restoration of Physiologic Balance.* It is here that selectivity must be employed by the physician. If the overactive thyroid dominates the picture then measures should be instituted to reduce and regulate thyroid activity.

If the opposite is present and a hypothyroid state, subclinical or true, as manifested by hypotension, asthenia, constipation, etc., is present, then measures for its correction are in order. Substitution glandular therapy is often productive of amazing results.

It is surprising how many patients will be found in this group. They have been on many and varied gastrointestinal regimes without success, but respond when the underlying factor is corrected.

In the group presenting the syndrome of underactivity of the adrenal, where there is a mild subclinical hypoadrenalinism or even a true deficiency, the response to adrenal cortex therapy is encouraging.

In the hypo-ovarian group the response to endocrine therapy is more than encouraging.

As mentioned previously, an underlying anemia, a focus of infection, any attendant ailment, must be adequately taken care of.

The effect of these deviations from normal in endocrine and sympathetic function upon the hydrogen ion concentration of the blood and of the acid-base equilibrium have been purposely omitted here.

Much in this endocrine and sympathetic system field is as yet unknown to us, but the great advances being made in the knowledge of the human body's response to environmental influence will in the coming years help us to solve these problems all the more successfully.



# A METHOD FOR REGULATING PRESSURE IN THE COMMON DUCT FOLLOWING CHOLEDOCHOSTOMY\*

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THE importance of the regulation of pressure in the common duct following choledochostomy has been emphasized by many authors.<sup>1,2,3</sup> Ravdin and Frazier<sup>4</sup> state that intense hyperemia with extravasation of blood into the liver tissue follows sudden release of tension. These authors point out that the maintenance of pressure on the common duct drainage tube forces part of the bile into the duodenum with resultant improvement in appetite and general well being. Despite the fact that bile draining from a liver damaged by common duct obstruction is deficient in bile acid,<sup>5,6,7,8</sup> it is of some advantage to conserve the bile as much as possible. The entrance of bile into the intestine avoids the necessity of instilling bile into the stomach through a tube which, at best, is bothersome and unpleasant to the patient. Furthermore, a saving of fluids and electrolytes is effected, which is a factor to be reckoned with when there is prolonged drainage of bile to the exterior.

Ordinary tube drainage into a bottle on the floor results in actual siphonage of bile from the common duct. Ravdin and Frazier avoid this by interposing a Y-tube, which is hung at any desired level at the bedside. Reid in 1921 stressed the importance of maintaining pressure on the drainage tube from the common duct and described a simple method for accomplishing this which is similar to that presented in this paper. We have found this method not only effective for maintaining pressure on the common ducts but advantageous in that it permits sterile collection and measurement of bile. We have found that the intravenous bottles and dispensing caps supplied with commercially prepared intravenous solutions supply the needed

equipment. Since many hospitals purchase intravenous solutions, these are usually available. All that is necessary is that a

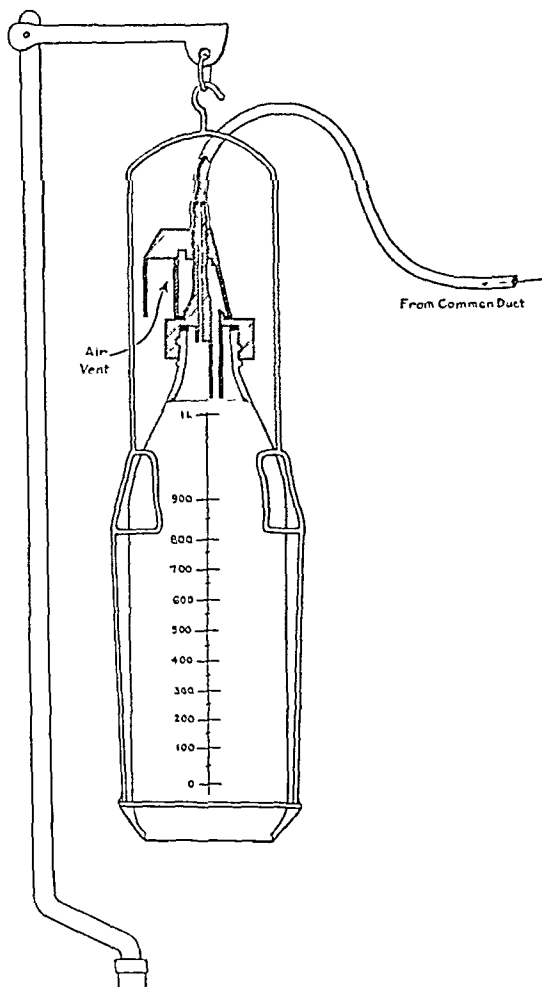


FIG. 1.

sterile bottle with an inlet tube and suitable vent be available. The collecting bottle may be placed at varying heights above the level of the common duct to regulate the pressure against which the bile must flow.

## DIAGRAM

The common duct tube is kept clamped until the patient is returned to bed. The

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tube is then attached to the intravenous set described above. The bottle is fitted into a wire basket, bottom down, and hung on an intravenous stand at the bedside. The level of the bottle can be regulated as desired on the intravenous stand.

The greatest advantage of this method is that no special apparatus is required. Clean, sterile intravenous sets are usually available. The bottles are frequently graduated so that the amount of drainage for any given period can be determined with ease, and the untidiness and odor associated with draining bile into open bottles on the floor is avoided. The height of the bottle in relation to the level of the common duct is easily adjustable and bile drainage can be obtained under sterile conditions. Samples can easily be obtained by exchanging bottles. Immediately postoperatively the bottle is hung a few centimeters above the level of the common duct and is then varied from day to day, depending on the

amount and character of the drainage and the patient's condition.

#### REFERENCES

1. REID, M. R. Drainage of the common bile duct through cystic duct. *Ann. Surg.*, 73: 458, 1921.
2. RAYDIN, I. S. Surgical problems in jaundice. *J. Med. Soc. New Jersey*, 23: 341, 1926.
3. JOHNSTON, C. G. Preoperative and postoperative treatment in cases of obstructive jaundice. *Surgery*, 3: 875, 1938.
4. RAYDIN, I. S., and FRAZIER, W. D. Gradual decompression following complete common duct obstruction. *Surg., Gynec. & Obst.*, 65: 11, 1937.
5. RAYDIN, I. S., JOHNSTON, C. G., RIEGEL, C., and WRIGHT, S. L. A study of human liver bile after release of common duct obstruction. *J. Clin. Investigation*, 12: 659, 1933.
6. BREUSCH, F., and JOHNSTON, C. G. Zum verschwinden und wiedererscheinen der Gallensauren in der Galle bei vorübergehendem choledochusverschluss. *Klin. Wchnschr.*, 13: 1856, 1934.
7. WALTERS, W., GREENE, C. H., and FREDERICKSON, C. H. Composition of bile following relief of biliary obstruction; report of series of illustrative cases. *Ann. Surg.*, 91: 686, 1930.
8. GRAY, H. K., BUTSCH, W. L., and MCGOWAN, J. M. Effect of biliary operations on the liver in relation to the concentration of bile acids in bile. *Arch. Surg.*, 37: 609, 1938.



# THE COMPARATIVE RESULTS OF PARTIAL EXCISION OF THE PANCREAS WITH THE SCALPEL, ACTUAL CAUTERY AND ELECTRICAL HIGH FREQUENCY KNIFE\*

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IN 1934, Dr. George Thomason,<sup>1</sup> in writing on the removal of a portion of the pancreas, stressed the point that that "to cut this organ with the cold knife is an unfortunate surgical error." To determine, if possible, the advantages

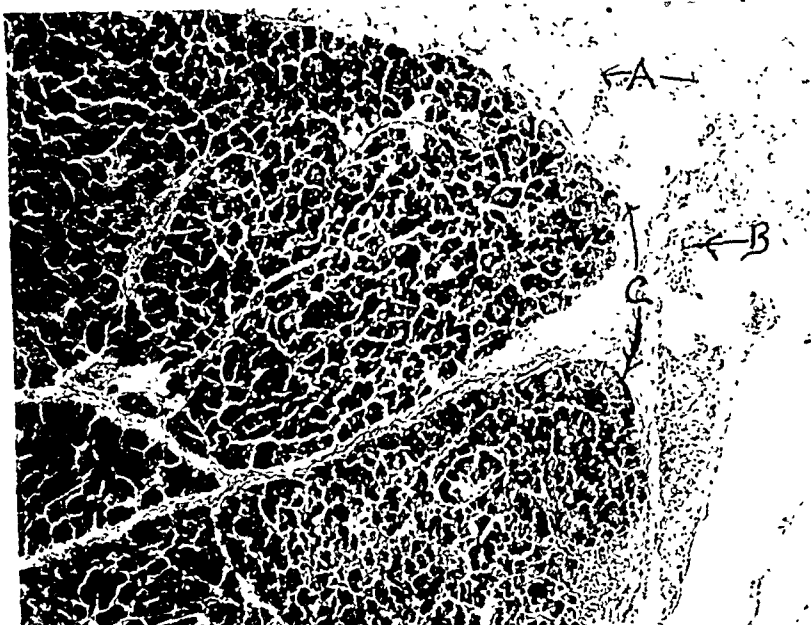


FIG. 1. Dog 1. Operation A. G.E. high frequency knife. Healed pancreas stump thirty-three days postoperative. A, loosely adherent omentum. B, connective tissue stroma. c, healed end of pancreas gland, conical shape, normal cells.

there is considerable advantage in the method of excision by means of the Percy cautery. Dr. Percy, in his discussion of this article, emphasized the value of actual cautery resection of the pancreas in overcoming the usually immediate hemorrhage as well as postoperative infection, both of which are possible when using the plain knife. He also points to another great advantage in the use of the cautery, namely, the prevention of postoperative pancreatic secretion from flooding the field. He states

or drawbacks of the respective methods was the aim of our experiments. Any advantage due to control of bleeding during the progress of the operation we have not considered because in the dog the blood vessels are so few and easily controlled by any method used that in our opinion it was not a point worth stressing.

We used dogs as subjects because the dog's pancreas is horseshoe-shaped with one rather long limb along the stomach, and the shorter distal limb along the duodenum, the main duct entering the

<sup>1</sup> *Tr. West. Surg. A.*, p. 85, 1934.

\* From the Department of Surgery, St. Louis University School of Medicine.



duodenum near the convexity or apex of the U-shaped gland. The head portion has a fairly loose attachment along the distal

or physiologic reaction of an individual animal to any one method, we used all three successive methods in animals 1 and

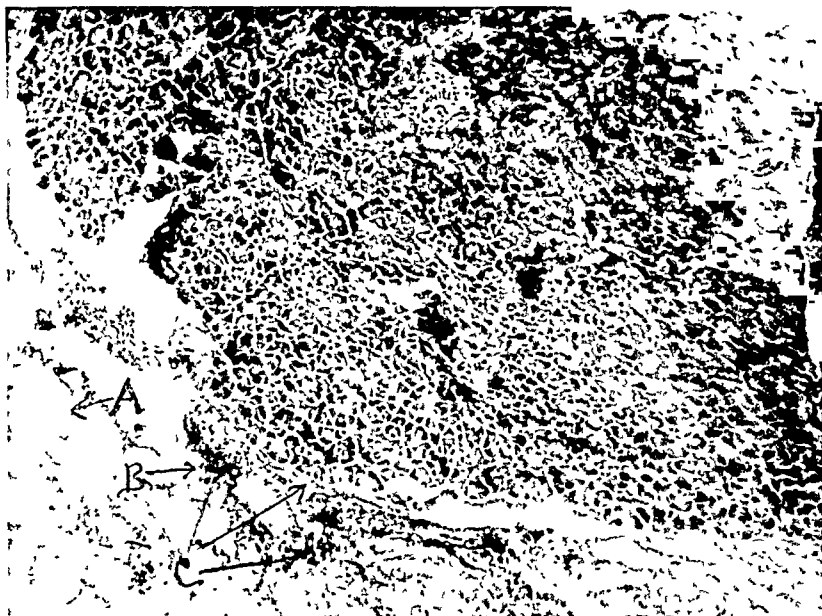


FIG. 2. Dog 1. Operation B. Actual cautery excision. Healed pancreas stump fifty-eight days postoperative. A, adherent omentum over stump end with excess fat. B, excess fibrous connective tissue. C, healed end of pancreas with islands of normal pancreatic tissue in the scar.

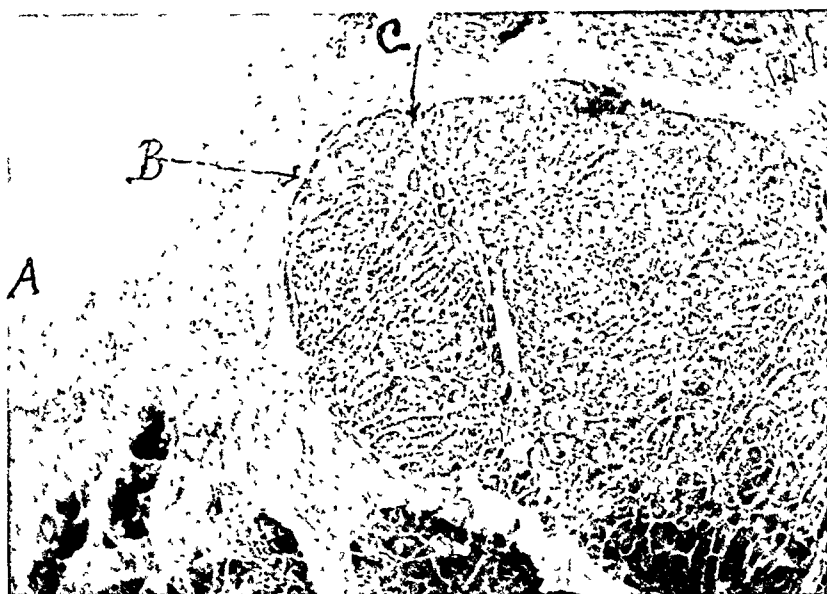


FIG. 3. Dog 1. Operation C. Scalpel scar. Healed pancreas stump eight months postoperative. A, fat containing leucocytes. B, fibrous connective tissue stroma. C, healed end of pancreas gland, normal ducts, slightly swollen island tissue cells.

part of the duodenum, and easily lends itself to a single or to several excisions. In order to overcome any possible pathologic

4. Regardless of the method used, the scars of the second and third excisions on the same pancreas had slightly more

adhesions about the stump than did the first excision.

The same technique of operating was

1 c.c. of 2 per cent solution per kilo of body weight, one hour before operation. Ether was then given on the open mask to the

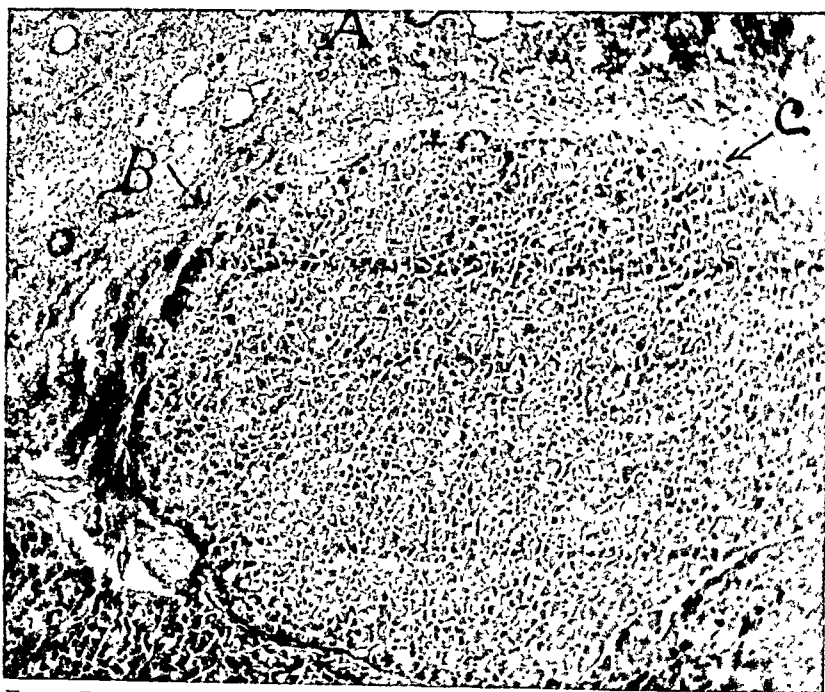


FIG. 4. Dog, IV. Operation B. Actual cautery. Healed pancreas stump twenty-eight days postoperative. A, well healed omentum. B, uniform fibrous connective tissue stroma. C, smooth rounded end of pancreas gland.



FIG. 5. Dog V. Operation A. Scalpel scar. Healed pancreas stump two months postoperative. A, omentum. B, thin fibrous tissue covering of stump. C, healed end of pancreas gland, conical shape, with normal cells.

used in all the dogs. The animal was given a preliminary dose of morphine sulfate,

point of complete anesthesia and then an intratracheal tube was used. On dogs 1 and

Dog No.	Weight in Kilo	Operation No.	Date	Method	Date Examined	Pathologic Report	Gross Appearance
1	12	1	1/15/35	G.E. electrical knife	2/28/35	The stump end is covered with fat. No scarring. The pancreas and ducts appear normal.	Omentum loosely adherent to stump. No other adhesions.
1	12	2	2/28/35	Actual cautery	4/27/35	There is an increase of fat and fibrous tissue over the cut end. There are some islands of pancreatic tissue in scar which look normal.	Omentum firm on stump end. Some adhesions about operative field.
1	12	3	4/27/35	Scalpel	12/17/35	Surface of stump covered with fat and fibrous tissue. Few leucocytes in fat. There is a definite increase in the lobules of the pancreas. Island tissue very abundant. Cells rather swollen. Ducts appear normal. Not much inflammatory reaction about the sutures in this specimen.	There were moderate adhesions about the stump, but none elsewhere and no evidence of other tissue degeneration.
2	..	1	12/22/34	Cautery	3/2/35	.....	Omentum over stump moderately adherent. Only a few adjacent adhesions.
2	..	2	3/2/35	Scalpel	3/5/35	Early healing over stump. Some evidence of early infection. Many pancreatic cells over free border are undergoing necrosis.	Dog chewed wound open. Numerous fibrinous adhesions. No pus. Specimen several hours post-mortem.
3	10	1	2/19/35	Cautery	4/20/35	In the end of the stump are some degenerative changes in the pancreatic tissue covered by the usual amount of fat and connective tissue.	Omentum firmly adherent to stump end with moderate adjacent fibrous adhesions.
3	10	2	4/20/35	Scalpel	.....	.....	Moderately firm omental adhesions over stump. No adhesions to intestine.
4	7	1	12/15/34	Scalpel	3/30/35	Stump is covered by thin layer of fibrous tissue. No fat. Pancreas at edge is normal. Islands, tissue and ducts are well preserved.	Very slight attachment of omentum to stump. No other adhesions.
4	7	2	3/30/35	Cautery	4/27/35	The end of the pancreas is covered with fat and connective tissue. There are several areas of inflammation about the ligatures. There is some interlobular increase of connective tissue. The pancreas tissue looks normal.	Slightly firmer, many and more omental adhesions over stump than at operation.
4	7	3	4/27/35	Electrical knife	8/4/35	.....	Omentum loosely adherent to duodenum at operation site. Pancreas atrophic.

Dog No.	Weight in Kilo	Operation No.	Date	Method	Date Examined	Pathologic Report	Gross Appearance
5	..	1	2/5/35	Scalpel	4/6/35	Inflammatory reaction about ligatures with considerable scarring about stump. Pancreatic ducts and islands are normal.	Very few omental adhesions to stump.
5	..	2	4/6/35	Cautery	8/4/35	.....	Very slight amount of fibrous adhesions about stump. Smooth.
6	7	1	6/1/35	Electrical knife	10/6/35	Stump normal in healing. Not much fat and fibrous tissue. Pancreatic tissue normal.	Good smooth scar over stump with slight omental adhesions.
7	6½	1	6/1/35	Electrical knife	8/18/35	Developed mange.	Usual smooth flattened conical end with few omental adhesions to stump end.

4 three operations were performed; on dogs 2, 3, 5, 6 and 7 two operations were performed.

At each operation the abdomen was opened by an upper midline incision. The head end of the pancreas was found, brought out and 1 cm. of the tip removed at right angles to the long axis of the pancreas either by (1) scalpel, (2) actual cautery, or (3) by electrosurgical knife (high frequency). Bleeding points were then clamped and ligated with cotton thread. The pancreatic duct was never sought and never intentionally ligated. The stump was cut squarely across in every case. A bit of omentum was then sutured over the raw end with fine silk. The abdomen was sutured, the earlier cases with No. 2 twenty day catgut, and the later with fine silk or cotton thread and the wound covered with collodion.

The second and third operations were performed in the same way on the same animal after three to six weeks had elapsed. At each second or third operation the condition of the general cavity was examined for peritonitis, fat necrosis, presence of fluid or adhesions and findings were noted.

At the second and third operations about 1 to 2 cm. of the previously cut end

of pancreas with the omentum covering it were then cut away from the head end, so that blocks and sections could be made to show the microscopic appearance of the excision line.

Another segment 1 cm. long was removed by a different method from that previously used. The vessels were ligated, the stump was covered and the wound closed exactly as before.

Again after three to six weeks, the animal was operated upon and the observations made as at the second operation. If a third operation was done it was performed in a similar manner, making a total of about 3 cm. of pancreas removed from the head end. After three to six weeks the abdomen was again opened and examined as before, and the terminal centimeter of stump with omentum covering it was removed for microscopic study.

Without exception in the cases examined after three weeks or longer the stump had assumed the shape of a wedge with convex edge like the normal pancreas end, and no longer remained as a blunt, squarely-cut stump as left at operation.

All microscopic examinations were made in the Pathology Laboratory of the St. Louis University School of Medicine and reported by Dr. J. R. Roberts, Associate

Professor of Pathology, to whom we wish here to express our grateful thanks. The specimens were fixed in 10 per cent formalin solution. They probably showed less cell detail than if Zenker solution had been used. All sections were cut in the same relative plane, in the long axis of the pancreas (parallel with and as near as possible to its central duct) and in the shortest diameter of the ellipse shaped cross section of the dog's pancreas. Table 1 gives a detailed summary of the experiments. It will be noted that there is but little difference in the gross and microscopic picture after operation 1, regardless of the method of cutting used. On gross examination the only difference noted after operations 2 and 3 was that there were rather more adhesions about

the stump and relatively more pancreatic tissue after the third section as the gland is normally thicker there.

#### CONCLUSIONS

There is least bleeding after excision by cautery and less after excision by electro-surgical high frequency surgical knife than after excision by scalpel, but even after scalpel excision the bleeding is not a problem worth considering. Our observations never revealed any evidence of postoperative peritonitis, collection of pancreatic secretion or fat necrosis. The distal end of the pancreas heals equally well if covered by a bit of omentum, regardless of whether it is excised by the scalpel, actual cautery or electric high frequency knife.



# THE ROLE OF SPLENECTOMY IN DISORDERS OF THE SPLEEN

## REPORT OF A SERIES OF THIRTY-THREE COLLECTED CASES

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**S**PLENECTOMY was first performed by Fioravanti in 1549, and the first substantial series of cases (fifty-three) was reported by Adelman in 1887. During this era, wounds, abscesses, cysts, torsion of the pedicle, and enlargement due to malaria made up the list of disorders for which the organ was removed. Today, the aforementioned causes are of infrequent importance, and certain blood dyscrasias now lead the list of indications for splenectomy. These blood disturbances are collectively designated as the splenic anemias. Those which will command our attention are (1) chronic hemolytic anemia, (2) Banti's disease, (3) idiopathic purpura hemorrhagica, and (4) Gaucher's disease. Their progress leads to one or both of the following complications which may frequently overshadow the splenomegaly in the symptoms and signs they exhibit: (1) liver damage with jaundice and ascites; and (2) a chronic anemia which is either hemorrhagic or hemolytic in origin. The spleen is also removed for rupture of the organ and enlargement due to tumors, cysts, and, at times, syphilis and malaria.

Chronic hemolytic anemia was first described by Minkowski in 1900. Splenectomy produces dramatic results in this condition. The diagnosis rests on increased fragility of the red blood cells, reticulocytosis, increased excretion of urobilinogen in the urine, and icterus. Curiously enough, 60 per cent of these patients have gallstones. The anemia is progressive, but then is followed by disappearance of both jaundice and anemia, although the microcytosis and fragility of the cells remain. Frequently after splenectomy, the platelets rise to unusual heights and there is danger

of mesenteric or portal thrombosis with high fever, abdominal pain, and convulsions. This may subside spontaneously after a few days when the platelet count returns to normal. If severe, deep Roentgen therapy should be applied before thrombosis appears.

Banti's disease is characterized by a progressive anemia with splenomegaly, leucopenia and thrombocytopenia. This same triad may be produced by certain acute and chronic infections, hemolytic anemia, Cooley's disease, leukemia, hepatic cirrhosis, and lymphoblastoma, and must be ruled out. As the disease progresses, hepatic cirrhosis with jaundice and ascites appears. Gastric and esophageal hemorrhages are quite common due to the subsequent engorgement of blood in the portal circulation. The prognosis depends then upon the amount of cirrhosis found at operation. Even in the late stages of the disease, splenectomy is quite justified on two scores: (1) the amount of blood in the portal circulation is reduced some 20 to 25 per cent, exerting a reduction of load on the scarred liver, and (2) the reduction of portal congestion obviates frequent gastrointestinal hemorrhages and resultant anemia. The liver in these cases has marked regenerative power. If the ascites is marked, one may perform an omentopexy in addition; and for repeated esophageal hemorrhage, coronary ligation is of definite value. If we are to accept Brandenburg's and Eppinger's conception that Banti's disease is not a separate clinical entity but merely a splenomegalic form of hepatic cirrhosis, we turn to the fact that W. J. Mayo performed splenectomy in some nineteen cases of true primary cirrhosis in

the last stages of the disease with good results. Present day management of cirrhosis permits more flexible medical treatment, while the ascites is handled surgically. The risk of splenectomy in Banti's may be somewhat greater than in the other splenomegalies due to the intimate nature of adhesions between the spleen and the diaphragm.

We caution against the advocacy of splenectomy in another disease entity which resembles Banti's. This is a splenomegaly with gastric hemorrhage but the splenic enlargement follows the hemorrhage within a day or two. These patients exhibit a portal thrombophlebitis quite commonly, and the spleen is thought to enlarge due to the stasis. Omentopexy and coronary ligation may be of considerable aid, but splenectomy gives deplorable results.

In purpura hemorrhagica idiopathica we have a comparatively rare disease, although symptomatic purpura is common, particularly in children. This disease was first described by Werlhof in 1735. About 80 per cent of those afflicted are females who have prolonged menses. There is a secondary anemia with a reduction of platelets. Subcutaneous and gastrointestinal hemorrhages are common; there is a prolonged bleeding time, delayed clot retractility, positive tourniquet test, and a normal coagulation time. Medical treatment is advisable in the acute phase of the disease as remissions are quite common. The only reluctance in delaying splenectomy is the frequency of intracranial hemorrhages following trivial trauma in these youngsters, when removal of the organ might have afforded a cure. After removal of the spleen the platelets rise to normal within the first week or so but do not remain there; however, hemorrhages are never so common or so severe as before splenectomy. Whipple reported seven deaths in eight operations performed during the acute phase, while there were only six deaths in seventy-three cases operated on during the chronic stage.

In Gaucher's disease we have a familial entity characterized by hemochromatosis, hypochromic anemia, leucopenia, thrombocytopenia and a later osteomalacia of bones with pathologic fractures. The spleen enlarges to great dimensions and there is deposition of kersin in the whole reticulo-endothelial system. Biopsy of the spleen or bone marrow reveals a characteristic lipoid laden pulp. Splenectomy is performed for symptoms produced by its enlargement, viz., pressure symptoms, severe anemia, or retardation of growth of the child.

Tumors and cysts of the spleen are relatively uncommon. Splenectomy is performed when exploration reveals their identity. One must remember that polycystic disease of the spleen may be associated with polycystic disease elsewhere.

Trauma is again becoming more important with the increase in auto accidents. Intraperitoneal hemorrhage with the history of a blow over the spleen should render suspicion of a rupture of the viscus. Splenectomy should be performed within the first twenty-four hours, as expectant treatment during this interval produces a 90 per cent mortality.

We have collected a series of thirty-three splenectomies performed in southeast Texas during the last ten years. In this group two were removed for hemolytic anemia with no deaths; ten for Banti's disease with three deaths; eight for purpura with four deaths; two for malaria with one death; three for leucemia with three deaths; one for lymphosarcoma of the spleen, and one incidentally to facilitate removal of a carcinoma of the stomach; and six for rupture of the spleen, with three deaths. (Table 1.) One patient with Banti's disease lived eight months, then succumbed from hepatic cirrhosis. One of the authors' cases of Banti's with grade 4 cirrhosis who was subjected to splenectomy with amentopexy has an apparent cure after four years. Another of our personal cases of Banti's gave a dramatic response to splenectomy and coronary ligation after multiple severe esophageal hemorrhages. We no longer

advocate removal of the spleen in the leucemias, as in doing so we would be removing the burial ground for the white cells which are already abnormally high.

TABLE I

Splenectomies	No.	Died
Chronic hemolytic anemia	2	0
Banti's disease	10	3
Purpura, idiopathic	8	4
Malaria	2	1
Ruptured spleen	6	3
Leucemia	3	3
Lymphosarcoma	1	0
Incidental to gastric resection	1	0
Total	33	14 (42.4%)

The total operative mortality of this group was 42.4 per cent which we think much too high. Splenectomy should carry a surgical risk of less than 10 per cent even in far advanced lesions.

#### CONCLUSIONS

1. Splenectomy is indicated in the treatment of the various splenic anemias, for

trauma, cysts, tumors, abscesses, torsion of the pedicle, and at times in syphilis and malaria.

2. Omentopexy and coronary ligation are to be performed in addition to splenectomy for the complications of the splenic anemias, viz., ascites and gastrointestinal hemorrhage.

3. A series of thirty-three collected cases is reported herein, exemplifying the indications for splenectomy. The combined operative mortality was 42.4 per cent.

4. The surgical risk of splenectomy even in late stages of disease should be less than 10 per cent.

#### REFERENCES

- BRANDENBURG, R. *Acta. chir. Scandinav.*, 59: 335-368, 1926.  
 BANTI, G. *Beitr. z. path. Anat. u. z. Path.*, 24: 21-36, 1898.  
 DIAMOND, LOUIS K. *Am. J. Surg.*, 39: 400, 1938.  
 EPPINGER, H., and RANZI, E. *Die Hepato-Lienalen Erkrankungen*. Berlin, 1920.  
 MAYO, W. J. *M. Rec.*, 92: 705-711, 1917.  
 OSLER, W. *Am. J. Med. Sc.*, 119: 54-73, 1900.  
 PEMBERTON, J. DeJ. *Ann. Surg.*, 94: 755, 1931.  
 WHIPPLE, A. O. *Surg., Gynec. & Obst.*, 42: 329-341, 1926.





# THE TREATMENT OF ENDOCERVICITIS WITH CARBON DIOXIDE SNOW (DRY ICE)\*

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**E**NDOCERVICITIS is one of the ailments which stubbornly resists medical treatment. The methods of therapy are legion. They may be classified as:

1. Biological: introduction of cultures of Doederlein bacilli into the vagina.

2. Chemical:

(a) Topical application of antiseptics in liquid, powder or paste form.

(b) Injection of chemical solutions under the cervical mucosa.

3. Thermal: Paquelin cautery.

4. Electrical:

(a) Nasal tip cautery.

(b) Coagulation.

(c) Conization.

(d) Ionization (copper, zinc, mercury).

5. Radium.

6. Surgical: Sturmdorf operation.

It is generally accepted that to cure endocervicitis one must destroy the diseased glands of the cervix. To achieve this it is necessary to sacrifice some of the surrounding tissues. One may easily accomplish this with any of the electrical methods. However, untoward sequelae may result:

1. Bleeding:

(a) Immediate—at the time of the procedure.

(b) Delayed—when the necrotized tissue sloughs.

2. Infection.

3. Cicatrization—causing stenosis or even complete atresia of the cervical canal with consequent sterility, cervical dystocia, hematometra and pyometra.

These unsatisfactory results not only militated against the indiscriminate use of the electrical methods but also prompted the search for a new necrotizing agent which would possibly avoid them. Such an agent belonging to the thermal group was found in the compressed form of carbon dioxide snow, popularly known as "dry ice."

Dry ice has a temperature of 109 degrees below zero. It is a dense, snow-like substance which evaporates to a dry gas.

Carbon dioxide snow as a therapeutic agent in medicine is not new. It was extensively used during the first decade of this century in various skin and eye diseases. Recently its use has been considerably curtailed due to the introduction and advancement of the various electrical methods. The destructive action of dry ice is ascribed to the rapid freezing and thawing of the treated areas. The cells rupture by expansion. The depth of necrosis is dependent upon the time of application and the pressure used. The cicatrization of the treated areas is minimal. It has been demonstrated that the epithelial cells are more sensitive to freezing than the connective tissue cells. This reaction resembles that of radium.

The following routine was worked out for the treatment of endocervicitis with dry ice.

The patient is placed in lithotomy position. A bivalve speculum is inserted into the vagina and the portio vaginalis is made visible and accessible. The vagina is wiped dry with cotton balls, the cervical canal with cotton applicators. No antiseptics and no anesthesia are used. The cervix is inspected and measured. An ice rod, long

\* From the Gynecological Department, Harlem Hospital, New York City.

and large enough to fill the cervical canal is cut from the ice brick. It will be found easy to cut the ice rod into the desired shape if a large kitchen knife, dipped from time to time into hot water, is used. The ice rod is grasped with a uterine dressing forceps at its widest end and introduced into the cervical canal as far as the internal os. Considerable pressure should be used during the application of the ice. As soon as the ice touches the cervix, the seething sound of the rapidly vaporizing ice will be audible and a dense gray gas will fill the vagina. This gas may be blown away and the actual freezing of the cervical tissue observed. In twenty or thirty seconds a white ring of natural ice will surround the dry ice stick. The seething sound ceases after fifty to sixty seconds and this indicates the end of the treatment. The dry ice may then be removed. By keeping the ice in the cervical canal for an additional ten to thirty seconds a prolonged treatment may be rendered. After withdrawal of the dry ice rod the natural ice will be visible in the cervical canal for about one minute. When the frozen area in the cervical canal melts the cervix will reappear in its former color and shape. Slight hemorrhage will fill the cervical canal. This bleeding is an indication that the treatment has reached the proper depth. If no bleeding occurs, the procedure should be repeated immediately. Before reintroducing the dry ice the cervical canal should again be wiped dry with cotton applicators. If an erosion is present, the dry-ice should be pressed against the eroded area. Treatment should not be repeated more often than once in four weeks. The freezing of the dry ice acts as an anesthetic agent and the patient as a rule experiences no pain during the treatment.

The after treatment consists of inspection of the cervical canal once or twice a week at which time tincture of iodine may be applied to the treated areas. The patient is instructed to douche with hot alkaline solution (two tablespoonfuls of

bicarbonate of soda to two quarts of hot water) whenever necessary for cleansing purposes.



FIG. 1. Biopsy taken twenty-four hours after treatment.

#### PRECAUTIONS

1. Do not handle the ice with bare hands. Burns may result. Always use a towel.
2. In cutting the ice with the knife, use a long sawing motion without pressure, as otherwise the ice will crack.
3. Use warm water for warming the knife; do not use a flame.
4. Do not touch the vulva or vagina with ice or the uterine forceps holding it, as this will cause pain.
5. It is unnecessary to use a tenaculum on the cervix.
6. If the ice breaks in the cervical canal do not try to remove it but allow it to melt in the canal.
7. Use considerable pressure! This is very important.
8. Tampons are unnecessary.

#### POSTOPERATIVE COURSE

The leucorrhea stops completely for twenty-four hours, following which it reappears, becomes milky and later watery in character. Seven to ten days after treatment the amount of discharge slowly dimin-

ishes. Normal cervicovaginal discharge with normal anatomic findings is observed in five to eight weeks. At this time the

general the picture is one of early regeneration, especially in the region of the stratified squamous epithelium. A conspicuous

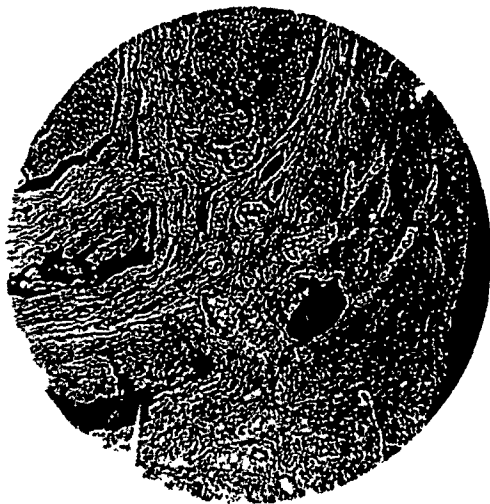


FIG. 2. Biopsy taken seven days after treatment.



FIG. 3. Biopsy taken sixteen days after treatment.

subjective symptoms disappear and the cure is complete.

#### CONTRAINDICATIONS

1. Microscopically proved malignancy of the cervix.
2. Acute external gonorrhea with predominant urinary symptoms.
3. Pelvic infections in the acute stage.
4. Pregnancy.

Palpable chronic adnexal masses were not considered as contraindications to the treatment.

#### PATHOLOGY

Inspection of the treated areas twenty-four hours after treatment shows them to be covered by a grayish pseudomembrane. This membrane is easily removable and consists of tissue debris mixed with mucus and pus cells. Under this membrane the red raw surface of the cervix is visible. The microscopic picture shows an extensive destruction of the cervical mucosa. (Fig. 1.) Seven days after treatment the areas are no longer covered by a pseudomembrane. The cervix bleeds readily to touch. Biopsies taken at this stage show areas of necrosis still present, but in

feature of the microscopic picture is the almost total absence of inflammatory changes. There is a moderate round cell infiltration; few plasma cells and a few leucocytes are present. (Fig. 2.) Ten to seventeen days after treatment macroscopic signs of healing are visible. Finger and v-shaped incursions into the areas of the erosion appear and the visible portion of the endocervix has the appearance of a granulating wound. Biopsy at this time shows a picture of active regeneration. The squamous epithelium is broadened, the stratum germinativum is wide, the nuclei are deeply stained. (Fig. 3.) Three to four weeks after treatment the entire area of the erosion is covered by stratified epithelium which has a marmorated appearance. Pale areas are surrounded by thin dark red lines. These lines disappear during the fifth or sixth week. The microscopic picture at this time reveals an increased activity of the stratified squamous epithelium. The stratum germinativum is still broad and the stratum corneum shows extensive vacuolization. The erosion appears in second stage healing. (Fig. 4.) Eight weeks after treatment cervical biopsy shows complete cure. (Fig. 5.)

During the microscopic study a very important finding was noted. In thirty-one cases out of 111 (30 per cent), atypical

5. Cases with atypical cells showed macroscopically a perfectly smooth normal cervical surface.

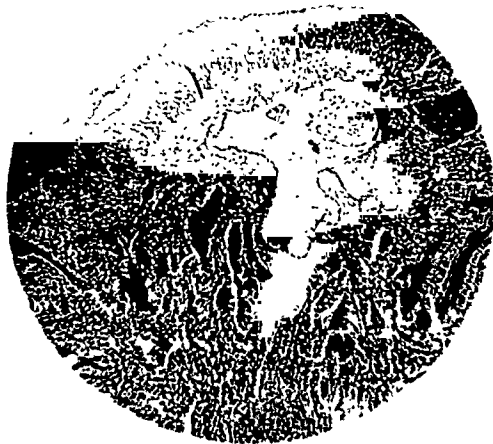


FIG. 4. Biopsy taken four weeks after treatment. Note atypical cells in surface epithelium.



FIG. 5. Biopsy taken eight weeks after treatment. Healed cervix.

cells were found in atypical arrangement, apparently invading the surrounding tissue. These findings resembled the earliest stages of cervical malignancy to such an extent that for a year ice treatment was suspended pending further study and follow up. Biopsies were taken from the cervixes of these patients at monthly intervals and the literature was carefully searched for evidence of carcinogenic properties of dry ice.

Two hundred and one biopsies were taken from the cervixes showing the atypical cells. The number of biopsies from the same individual varied from one to seven. The duration of observation ranged from one to two and a half years. On the basis of this follow-up the following statements may be made:

1. All cases had erosions prior to the ice treatment.
2. The number of ice treatments had no influence in the development of atypical cells.
3. The atypism was observed as early as one week after treatment.
4. The duration of the atypism ranged from three months to over two and a half years.

Berenblum in 1929 and 1930 published two articles dealing with his experiments with dry ice. He concluded that dry ice has no carcinogenic properties, either in animals or in human beings. Thus it appears that these nests of atypical cells have nothing in common with true malignancy. They may be regarded as signs of increased activity of the stratified squamous cell epithelium in a healing erosion.

## RESULTS

Three hundred and twenty five patients received ice treatment. The first was treated in May, 1934, the last in December, 1935. In the beginning, the action of dry ice was not thoroughly understood and the results were not uniform. The present routine was gradually worked out. Since its perfection the results have been gratifying. Seventy per cent of the patients required only one ice treatment for a cure. Cases with erosion responded more readily to the treatment. Fifteen per cent required two ice treatments, and 15 per cent were treated three or more times.

No postoperative sequelae such as bleeding, inflammation or stenosis of the cervical canal have been observed to date. No

patient required hospitalization. The discomfort to the patient was minimal.

These findings and observations recommend the treatment with dry ice as a good conservative procedure in the treatment of endocervicitis.

#### SUMMARY

1. Topical application of a dry ice rod to the cervical canal for sixty to ninety seconds is offered as a new method of treatment of endocervicitis.

2. Dry ice belongs to the thermal agents of treatment.

3. This method was used for eighteen months in 325 cases. The cases were observed for two and a half years.

4. The results were very gratifying especially where cervical erosions were present. Seventy-five per cent had such erosions.

5. In 70 per cent of the cases only a single application of dry ice was necessary; 15 per cent required two treatments; 15

per cent needed several applications to achieve cure.

6. The treatment with dry ice is simple and painless. No unfavorable sequelae were noted.

7. The area of destruction is limited.

8. The inflammatory reaction after ice treatment is surprisingly minimal, cicatrization is entirely absent.

9. Dry ice markedly stimulates the growth of the stratified squamous cells.

10. Atypical cells in atypical arrangement were observed in 30 per cent of the cases as a result of this stimulation.

11. Two hundred and one biopsies were studied for a period of two and a half years. No evidence of true malignancy was observed. This atypism is only a sign of accentuated activity on the part of the stratified squamous epithelium.

#### REFERENCES

1. BERENBLUM, I. *Brit. J. Exper. Path.*, 10: 179, 1929.
2. BERENBLUM, I. *Brit. J. Exper. Path.*, 11: 208, 1930.



# GRANULOMA VENEREUM (INGUINALE)\*

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**G**RANULOMA inguinale is a chronic inflammatory disease of disputed venereal origin, clinically characterized by ulcersclerosing lesion of the skin and mucous membranes of the genito-inguinal regions, and histologically by the presence of Donovan bodies in the monocyctic cells of the exudate.

In medical literature it has been variously designated as "granuloma pudenda tropicum," "granuloma genito-inguinale," "ulcerating granuloma," "granuloma venereum," etc. The term lymphogranuloma inguinale which applies to a different disease entity has led to considerable confusion.

The etiology of granuloma inguinale still remains unsettled. From 1882 to 1905, the lesion was frequently considered tuberculous.<sup>8-11</sup> Claims for spirochetal etiology were frequently made<sup>12-15</sup> until 1905, when Donovan reported intracellular organisms supposedly protozoa.<sup>16</sup> Now recorded in the literature as Donovan bodies, these structures are constantly associated with the disease and, though diagnostic, have not as yet fulfilled Koch's postulates. In this country, Symmers and Frost in 1920 were the first to recognize Donovan bodies in this lesion.<sup>17</sup> Other interpretations, however, have also been placed upon the nature of these inclusions. Siebert<sup>18</sup> and Martini<sup>19</sup> in 1907 interpreted them as diplococci. After cultural studies Aragao and Vianna<sup>20</sup> interpreted them as schizomycetes. In 1917, Walker<sup>21</sup> and later Randall, Small and Belk<sup>22</sup> and others viewed them as *Bacillus mucosus capsulatus*. Castellani and Mendelsohn<sup>23</sup> in 1929 cultured Gram-negative organisms possessing morphologic characteristics of Donovan bodies, but did

not consider them as the true cause of the disease, for inoculation produced only purulent lesions. MacIntosh<sup>25</sup> transmitted the lesion in the human by tissue graft and from such sites Donovan bodies were found on smear and culture. He believes the Donovan body to be the cause of the disease and excludes a filtrable virus.

Clinically, the disease is characterized by extreme chronicity and the absence of any tendency towards spontaneous healing. Although rectum, vagina, urethra, mouth and pharynx have been attacked, the disease shows a predilection for the external genital organs and perianal regions. In the female it often invades the vagina but only rarely has the cervix been affected. Pund and Greenblatt<sup>25</sup> very recently recorded two patients with involvement of the cervix uteri, one erroneously treated as carcinoma until pathologic study was made. Pund and Gotcher<sup>26</sup> have reported cases involving uterus, tubes and ovaries.

The period of incubation is varied. Cases with only two days' interval from the time of sexual contact are on record, others extend to three months. There are rarely any constitutional symptoms in this interval or after the appearance of the lesion. Locally, there is little pain though disturbances vary according to the organ involved, e.g., rectum, vagina, etc. Chafing, a burning sensation and itching are generally described.

Though most common in tropical countries, granuloma inguinale is not rare in the United States.<sup>1,2</sup> It occurs as a rule during adult life, but cases are recorded in children of 2 and 6 years.<sup>3,4</sup> A rare case reported by Scott<sup>5</sup> was found in a 67 year old male. Racially negroes predominate, probably

\* From the Gynecological Department, Brooklyn Cancer Institute.  
Read before the Brooklyn Gynecological Society, December 2, 1938.

the result of lack of sex hygiene rather than any special predisposition. Sexual congress is believed to be the underlying cause.

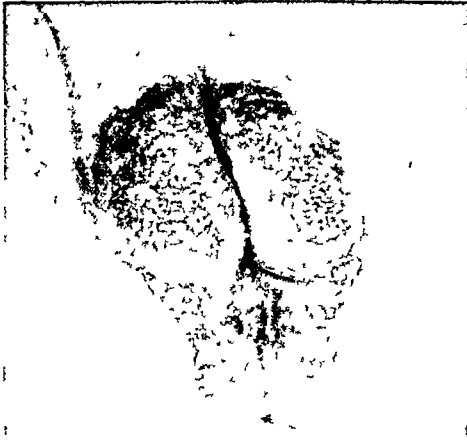


FIG. 1. Case 1. Gross appearance of the hypertrophic form of granuloma inguinale. Both labia are the seat of firm papillary and bulbous elevations. Superficial ulcers are present. Note the posterior butterfly extension onto the buttocks.

D'Aunoy and von Hamm,<sup>27</sup> whom we freely quote below, excellently describe the gross features and divide them into three groups. Group 1 lesions, caused primarily by the infectious agent, comprise nodular elevations and serpiginous ulcers. The nodules are usually only the beginning stage of infection and undergo further changes which lead to development of the serpiginous ulcer, the most common and most typical manifestation of the disease. The lesion is characterized by a soft, easily bleeding granulation tissue which breaks through the epithelial lining of the skin and mucous membrane and shows a remarkable tendency towards superficial spread along the moist folds of the inguinal and pudendal regions (Manson). These lesions are only a few millimeters deep and usually show very little suppuration. The exudate is serosanguineous, contains the infectious agent and spreads the disease by auto-inoculation. The rapidity with which the infection spreads varies considerably and healing may be observed in some portions of the lesion while other parts show continuous encroachment upon sound tissue.

During the course of the disease considerable areas of the skin and mucous membranes are usually covered with these ulcerative lesions, with resultant severe anatomic mutilation of the genitalia and the perineum. The healing process is slow and the scars produced are atrophic with partial depigmentation of the skin and permanent loss of hair.

The second group of pathologic manifestations is the result of a peculiar host reaction to the infectious agent, leading to hypertrophic and keloid-like lesions. The surface of the hypertrophic lesions may be compared to the relief map of mountainous country, with depressions between areas of piled up tissue. In consistency the lesions are firm and rather elastic, the overlying skin usually showing scars of previous ulcerations. There is often very little difference between this type of lesion and the true cicatricial or keloid-like lesion. In the latter there is an apparent over-production of firm, indolent tissue which replaces the ulcerations. This is not a healed stage of the disease, but a progressive lesion, as confirmed by the fact that the histologic examination shows the presence of Donovan bodies in the small nests of inflammatory cells embedded in the dense collagenous fibrous tissue obtained from such scars.

The third group of pathologic manifestations of granuloma inguinale consists of the lesions that occur as complications of the primary infection. The most frequent is secondary infection with aerobic or anaerobic pyogenic or saprophytic organisms. The onset of a virulent secondary infection is usually characterized by the appearance of toxic constitutional symptoms which are completely absent in the uncomplicated forms of granuloma venereum and by progression of the ulcerative process with the production of deep severe necrosis of soft tissues and even bone.

Microscopically, granuloma inguinale reveals in the pure or unmixed cases a uniform histologic picture. The essential features are: (a) hyperkeratosis which may be adjacent to areas in which the surface

epithelium is becoming ulcerated; (b) acanthosis; (c) elongation of the rete pegs; (d) dyskeratosis of the accelerated type

structure. Atypical forms, such as non-encapsulated bacillary or diplococcoid forms surrounded by a zone of rarefaction and



FIG. 2. Case 1. Histology of granuloma inguinale ( $\times 120$ ). The surface epithelium shows hyperkeratosis. Elongation of the rete pegs with parakeratosis and suggested pearl formation are dominant characters. The underlying connective tissue contains the inflammatory exudate.

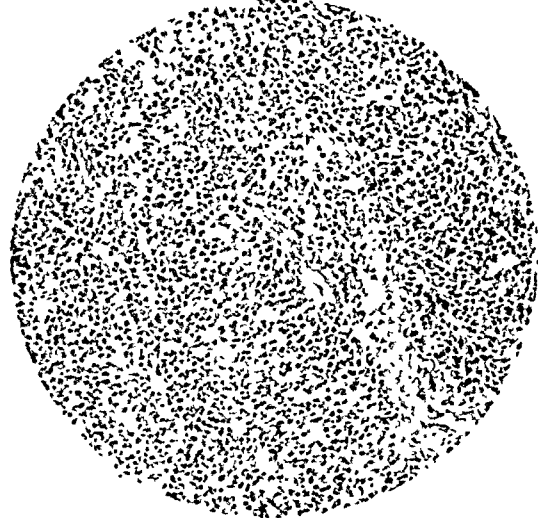


FIG. 3. Case 1. The inflammatory exudate in granuloma inguinale is predominantly of the plasma cell type. Monocytes, lymphocytes and occasional neutrophils are also encountered. ( $\times 120$ .)

which in some areas is such as to suggest pearl formation; (e) a nonspecific inflammatory infiltrate in the corium, in which plasma cells abound though neutrophils and small round cells may be present; (f) varying amounts of fibrous tissue deep in the lesion; and (g) the pathognomonic cell with inclusion Donovan bodies.

The pathognomonic cell is most distinctive. It is a relatively large monocyte varying from 25 to 90 microns in diameter. The many intracytoplasmic cysts are filled with deeply stained bodies varying from .5 to 2 microns. These bodies as seen with hematoxylin-eosin are round or rod-like and are grouped peripherally within the cysts. They show strong affinity for this dye. In smears stained by Wright's technique the Donovan bodies show an unstained or feebly stained body with a centrally placed bacillus-shaped or minute coccoid chromatin body and a distinct well stained capsule. The central body may also appear as diplococcoid or diphtheroid in

zooglear forms, are frequently seen. The varied interpretations of the organism's nature may be easily explained by this pleomorphism. The silver stain in tissue simplifies identification of the organisms.

The diagnosis in spite of the characteristic gross appearance is not simple. Chancroid, however, is easily differentiated. This is an acute disease, painful and associated with buboes. The ulcers are phagedenic and frequently yield to local treatment. Durey's bacillus may be found on smear. Tuberculosis is excluded only on microscopic appearance. The finding of tubercle formation and demonstration of tubercle bacilli are conclusive. The coexistence of syphilis and granuloma inguinale may be misleading. The presence of treponemata in the chancre or the classical microscopic appearance of gumma easily establish lues. In doubtful cases response to arsenical therapy is diagnostic. In the external genitalia, granuloma inguinale is frequently diagnosed as carcinoma. The two cases reported here were seen in a cancer hos-



pital. Vulvar carcinoma as well as cancer of the skin in general, however, is rare in negroes who are so frequently subject to

antigen obtained from suppurating lymph nodes or from the virus-infected mouse brain (Frei test) is specific for lympho-

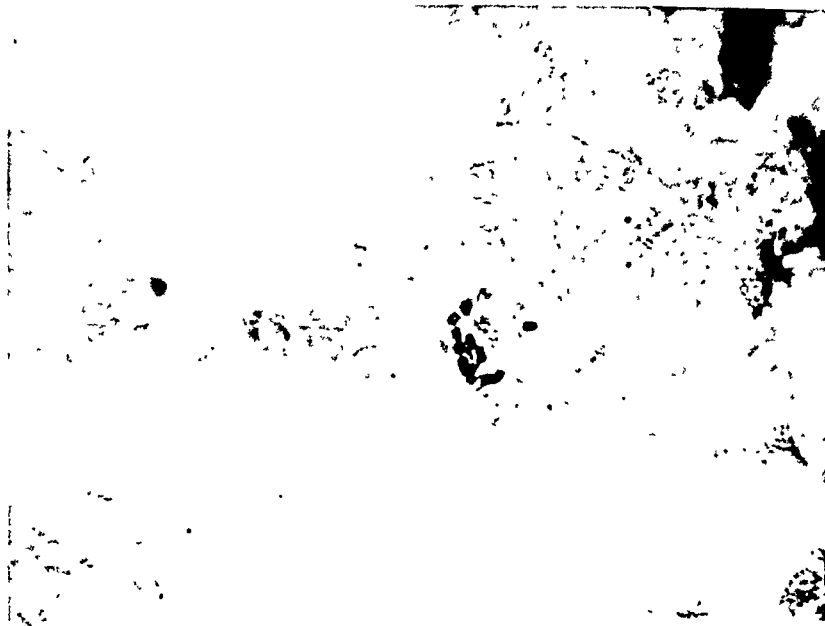


FIG. 4. Case 1. A group of intracellular Donovan bodies heavily impregnated with silver. Their oval form and peripheral accentuation of stain are characteristic. ( $\times 2200$ .)

granuloma inguinale. In carcinoma there are often vestiges of leucoplakia. Absence of lymph node enlargement in granuloma inguinale is especially striking when considering the wide extent of the local lesion. The microscopic picture is of course distinctive but hyperplastic and acanthotic changes in granuloma inguinale may sometimes lead to confusion.

Lymphogranuloma inguinale or lymphopathia venereum is most frequently confused. Clinically, lymphogranuloma inguinale is a disease of the lymph nodes and lymphatic channels while granuloma inguinale is a disease of the skin and subcutaneous tissues. The primary lesion in lymphogranuloma inguinale is rarely encountered on the external genitalia. The vagina or cervix are the primary seat. The initial lesion heals quickly so that it is seldom found. Enlargement and suppuration of the inguinal lymph nodes is frequently the first finding. In late cases a stricture of the rectum is encountered. The positive cutaneous response to injected

granuloma inguinale. Even in cases where ulceration of the skin or genitalia appears, lymphogranuloma inguinale is identified by its microscopic appearance and the Frei test. Donovan bodies are lacking. The specific response to antimonials in granuloma inguinale may also be used as further diagnostic evidence. We again emphasize the use of silver stain for identification of Donovan bodies in biopsy specimens.

Treatment in the early days of the disease consisted of radical surgical extirpation of the lesion. Local recurrences, however, were the rule. Coagulation,<sup>28</sup> x-ray therapy,<sup>20</sup> vaccines,<sup>30</sup> have all been employed. Antimony, which is a specific cure for granuloma inguinale, was first employed by Aragao and Vianna of Brazil. Tartar emetic given intravenously is advised, beginning with 2 c.c. of a 1 per cent solution in distilled water, slowly increasing the dose until 10 c.c. is reached. Injections are given every second to third day and continued weekly for two to three months after healing has occurred to prevent local

recurrences. It is believed that not more than twenty to thirty injections should be given in a course. Nausea, dizziness, bone

itching and a bleeding sore in the region of the external genitals. Symptoms had begun six months prior to her visit and had become

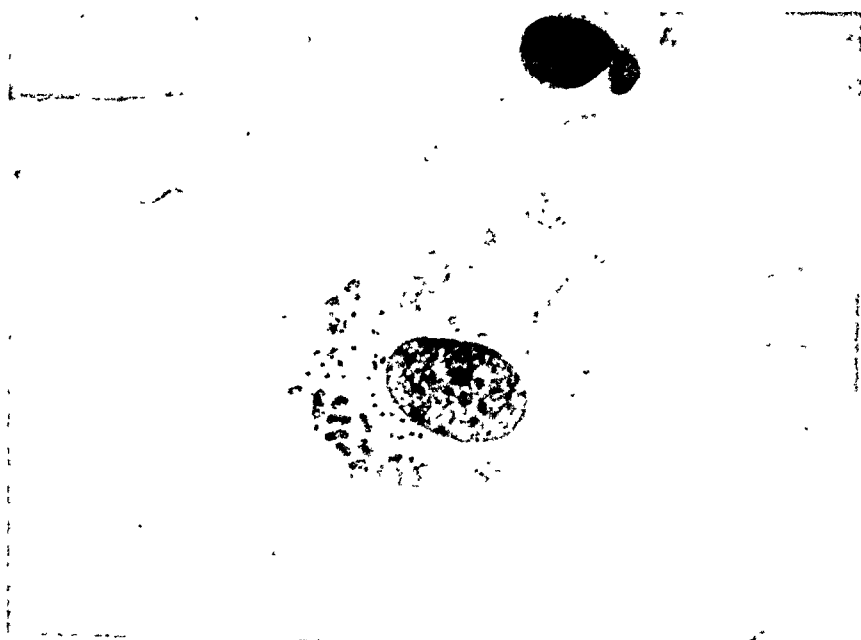


FIG. 5. Case 1. A monocyctic cell, large and containing a deeply staining oval nucleus. The cell cytoplasm contains many vacuoles. At the periphery of the cell are classic Donovan bodies. They present a well stained capsule with central coccoid, diplococoid and bacillary structures. ( $\times 1870$ .)

pain or diarrhea may necessitate a temporary halt.

More recently a newer antimony compound has become available which can be used intramuscularly.<sup>31</sup> This drug, called fuadin, was first introduced by Khalil of the University of Cairo for the treatment of bilharziasis. It was first employed for granuloma inguinale by T. V. Williamson in this country in 1933.<sup>32</sup> Fourteen cases were reported in his series with excellent results. Treatment begins with 1 c.c. of the drug administered intramuscularly, increasing the dose until 5 c.c. is employed. Injections are given two to three times a week until healing occurs. In rare cases where antimony is contraindicated or produces no results, surgery, x-ray or coagulation must be resorted to.

#### CASE REPORTS

CASE 1. Mrs. J. J., age 55, mulatto, was first seen in the gynecological department in October, 1935 when she complained of vulvar

progressively worse. The itching was so severe that rubbing and scratching for relief were almost constant. Later, white pimples appeared which broke down, bled, became red and increased in size. A discharge was also present and both symptoms were aggravated by walking. She had had sexual intercourse with a West Indian six weeks before the appearance of her complaints. There was no other exposure and the family and past personal history were otherwise negative. She denied lues and gonorrhea.

Examination revealed a granular elevated lesion which involved the labia majora and minora on each side, extending from the clitoris to the fourchette. (Fig. 1.) There was also butterfly extension toward the anus and on the posterior vaginal wall for 1 inch. The surface of the lesion presented fine granular excrescences and also round or ovoid nodules. Focally there were zones of superficial necrosis from which a fetid serosanguineous fluid exuded. In the posterior extension the external surface of the lesion was smoother but its demarcation from healthy skin was sharply indicated by a raised indurated margin. The inguinal nodes were not enlarged.

Several biopsies were taken which were variously reported as dyskeratosis, with marked inflammation and prickle cell carcinoma. The



FIG. 6. Case 11. The labium minus partially destroyed by a granulomatous ulcer with a thickened serpiginous margin. Two smaller ulcers just anterior to the anus are also shown.

Frei test and Wassermann examinations were negative. The blood count was normal. Smears studied for Donovan bodies at this time were erroneously reported as negative. A diagnosis of granuloma inguinale was made but since several observers believed the lesion to be carcinoma of the vulva, the patient was admitted for operation on December 3, 1935.

The vulva was first treated with antiseptic dressings of acriflavine for disinfection of the wound for a period of twelve days. On January 15, 1936, vulvectomy was performed under ether anesthesia. The postoperative course was uneventful until the fourth day when beginning necrosis required removal of the sutures. Acriflavine dressings were reapplied and healthy granulations became apparent on the tenth day. On the twenty-first day postoperative, due to tardy healing, 5 c.c. of fuadin were given intramuscularly and continued twice weekly. Healing then progressed more satisfactorily and upon discharge from the hospital on March 6, epithelization was well advanced, but edema of the right labium was present. Fuadin was continued every fourth to seventh day, for a

total of fifteen injections. Although healing was complete, the lymphedema of the right labium persisted and was treated by x-ray therapy from June 15 to June 29, 1936. One hundred fifty radiation units were given every second day, until 750 R. units were administered. The factors were: 40 cm. S.T.D., 200 Kv., 5 M.A.;  $\frac{1}{2}$  mm. copper and 1 mm. Aluminum filters.

On September 15, 1937, twenty-one months after operation, a recurrent ulcer 2.5 cm. in diameter appeared on the right buttock just a little below the anus. Nine injections of fuadin were given, starting with a dose of 1.5 c.c. and increasing the quantity until 5 c.c. were administered. Six weeks later the lesion was entirely healed. The patient seen early in 1938 was clinically well.

The pathologic report of the operative specimen showed that the epithelial layer was the seat of areas of hyperkeratosis and dyskeratosis, the latter resulting in marked hypertrophy of the rete pegs with extension deep into the dermis. (Fig. 2.) There was no evidence of malignant change of the cells of the epidermis. The cutis and the subcutaneous structures were involved in a marked and extensive exudate. The plasma cell predominated but lymphocytes and monocytes were encountered. (Fig. 3.) There was a superimposed acute inflammation accompanied by ulceration of the epidermis, at which sites the acute inflammatory exudate replaced the superficial layers of the epidermis. The conclusion was that the case was one of granuloma, with superimposed acute inflammation and ulceration. Reexaminations of the excised operative specimen and the biopsy tissues were made with the Dieterle silver method (Fig. 4) and typical Donovan were easily disclosed. Smears from the recurrent lesion in 1937, stained by the Wright method, also showed the organisms. (Fig. 5.)

The lesion in this case was of the nodular type. Despite widespread involvement of the vulva and inguinal zones, the lymph nodes were not involved. Surgical excision was not entirely satisfactory, but there was prompt healing of the operative site after the use of fuadin. A recurrence twenty-one months after operation also responded quickly to the use of this agent. The diagnosis of granuloma inguinale was easily made in the operative and earlier biopsy specimens during their restudy. The silver stain was especially helpful in find-

ing the classical Donovan bodies in excised tissues.

CASE II. Mrs. M. H., age 54, colored, was

2 or 3 mm. and covered with a scant, sero-sanguinous, foul discharge. The edge of the lesion was sharply defined, thickened and

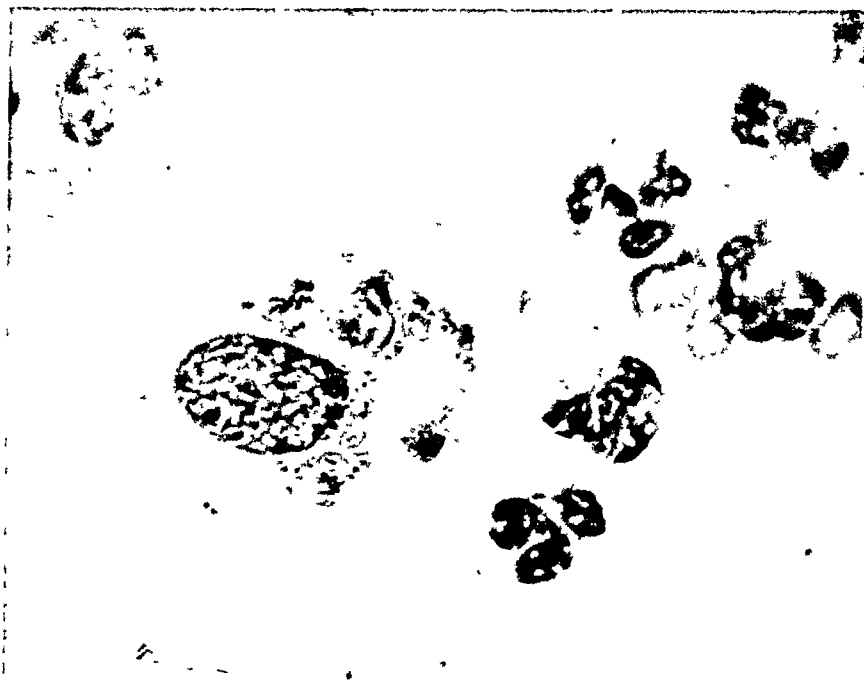


FIG. 7. Case II. The large deeply stained nucleus of a monocyte is clearly shown. The cell cytoplasm is hardly visible. Mature Donovan bodies, irregularly distributed, show a well defined capsule with central diplococcoid, bacillary and diphtheroid formations. ( $\times 2100$ .)

first seen in May 1937. She complained of itching and a sore on her vulva and groins present since 1935. Coitus in the past six years was denied. The sore started as a pimple near the vulva and gradually increased in size. There was no pain. The lesion was interpreted as luetic in origin because of a positive Wassermann and a series of salvarsan injections was given but without result. The patient was accordingly referred by the Health Department to the Brooklyn Cancer Institute in 1936 for a biopsy. A pathologic diagnosis of pyogenic granuloma was made and the patient returned to the Board of Health for continued observation and luetic treatment. No improvement was obtained. In May 1937, the gynecologic examination showed the following: the right labium minus was partly destroyed by a granulomatous ulcer which extended from a point just below the clitoris downward for about 4 cm. (Fig. 6.) It was irregular in outline and measured  $4 \times 3$  cm. Laterally it reached the labium majus and medially encroached upon the introitus and vagina. The floor of the ulcer was somewhat granular, elevated about

rolled. It was distinctly serpiginous. On the fourchette, just anterior to the anus, were two additional small lesions about 1.5 cm. in diameter, having similar characteristics. In the right groin, there was an oval lesion  $3 \times 2.5$  cm. whose center was more elevated. The edge of the lesion had the same characteristics, but was not serpiginous. Below this area, there was a healed depigmented scar. In the left groin there was a cord-like thickening but distinct nodes could not be palpated in either groin. The vagina and cervix were normal. Except for two external hemorrhoids, rectal examination was negative.

The Wassermann and gonococcus fixation tests were negative. Injection with Frei antigen produced a positive nodule 12 mm. in diameter. The blood count was negative except for moderate eosinophilia. Urine examination was negative. The sedimentation time was 25 minutes. Smears from the ulcer stained by Wright's method were positive for Donovan bodies. (Fig. 7.)

The first biopsy, taken in 1936, showed tissue covered by a thickened, stratified squamous

lining epithelium infiltrated by polymorphonuclear cells. Beneath this there was a rich leucocytic infiltrate containing numerous neu-

In this case there was a coexistence of a positive Wassermann, positive Frei test, and positive smear for Donovan bodies.

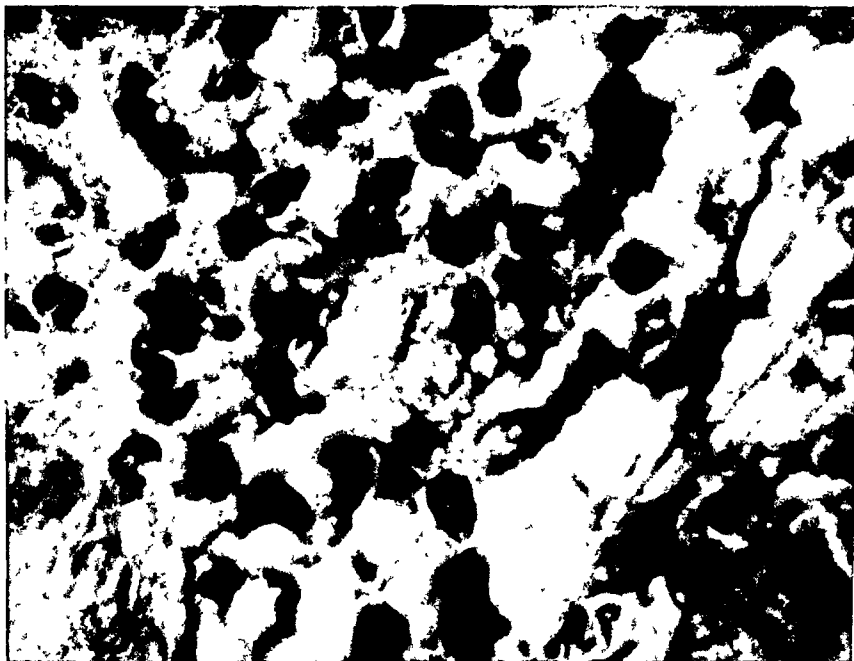


FIG. 8. Case 11. A large monocyte lies in the center of the field. The deeply staining nucleus is eccentrically placed. The cell cytoplasm presents characteristic multiple cysts. Donovan bodies are present though poorly reproduced in the photograph. ( $\times 2000$ .)

trophiles and plasma cells. Areas of necrosis and pycnotic nuclear debris were intermingled. Collections of young connective tissue cells were frequent. In our restudy with hematoxylin and eosin and Dieterle techniques, Donovan bodies were found in the monocytic cells of the exudate. (Fig. 8.)

Fuadin therapy was administered by intramuscular injections. On May 8, 1937, 1.5 c.c. was given, followed by 5 c.c. on May 11, 14 and 15. On May 18, the margins of the vulvar ulcers were noted to have flattened out, and the edges were less distinct. The bases soon appeared as smooth pale pink areas covered with a thin secretion. The groin lesion was also smaller but did not show such prompt regression. The patient left the hospital and was referred to a private physician for observation. In November, 1937, the lesions were entirely healed with the formation of depigmented scars. Repetition of the Frei test in November, 1938 showed a large papule, indicating the coincidence of lymphogranuloma inguinale with granuloma inguinale or a repeated false positive reaction for lymphogranuloma.

Salvarsan therapy produced no effect on the classical ulcerative type of lesion. Absence of enlarged lymph nodes and prompt response to fuadin excluded lymphogranuloma as the cause of the vulvar lesion. Early pathologic study failed to show the etiology of the lesion, but re-examination of the tissue two years later by the silver technique showed numerous Donovan bodies which were also present on smear examination. The rapid response to the small amount of fuadin was striking.

#### CONCLUSIONS

1. Granuloma inguinale is a chronic inflammatory lesion of the skin and subcutaneous tissues. It occurs most frequently in the colored race. The genito-inguinal region is the site of predilection. It appears in hypertrophic and ulcerative forms which are often mistaken for carcinoma.

2. Extensive vulvar lesions with absence of enlarged regional lymph nodes is clinically characteristic.

3. Pathologic reports on such lesions are often erroneous or incomplete, yet the microscopic picture is distinctive. The finding of Donovan bodies is conclusive.

4. A search for these bodies should be made in all genito-inguinal lesions presenting the clinical and pathologic features described. Smears and tissue sections show the organisms.

5. The Dieterle silver stain is a great aid in the microscopic diagnosis of Donovan bodies in excised tissues. The Wright technique is similarly satisfactory for examination of smears.

6. The use of antimony is specific and fuadin is the ideal drug.

#### REFERENCES

1. HARRIS. *Laryngoscope*, 40: 707-737 (Oct.) 1930.
2. FOX, HOWARD. *J. A. M. A.*, 87: 1785 (Nov. 27) 1926.
3. COLE, MISKJIAN and RAUSCHKOLB. *Dermat. Ztschr.*, 53: 127-143, 1928.
4. DE MATTA, A. A. *Gac. med. Venezuela*, 1916.
5. RANDAL, A. J. *Urol.*, 9: 491-504, 1923.
6. SCHOCHET, S. S. *Surg., Gynec. & Obst.*, 38: 759-766 (June) 1924.
7. NAIR, G. C., and PANDALAI, N. G. *Indian M. Gaz.*, 69: 361-371 (July) 1934.
8. McLEOD, K. *Indian M. Gaz.*, 17: 120-122, 1882.
9. CONYERS and DANIELS. *Brit. Guiana M. Ann.*, p. 113, 1896.
10. LE DANTEC. *Précis de pathologie exotique*. Paris, 1900.
11. JEANSELME. *Cours de dermatologie exotique*. Paris, 1904.
12. WISE. *Brit. M. J.*, 1: 1274, 1906.
13. BOSANQUET. *Parasitology*, 2-4, 344.
14. MACLENNON, A. *Brit. M. J.*, 2: 995, 1906.
15. CLELAND, J., and HUKINBOTHAM. *J. Trop. Med. & Hyg.*, 10: 142-151, 1909.
16. DONOVAN, C. *Indian M. Gaz.*, 40: 411-414, 1905.
17. SYMMERS and FROST. *J. A. M. A.*, 74: 1304-1306, 1920.
18. SIEBERT, W. *Arch. f. Schiffs. u. Tropenbug.*, 12: 12, 1908.
19. MARTINI. *München. med. Wchnschr.*, p. 2378, 1912.
20. ARAGAO, H. DE B. *New Orleans, M. & S. J.*, 70: 369-374, 1917. *Mem. D. Inst. Oswaldo Cruz*, 11: 211, 1913.
21. WALKER, E. L. *J. M. Research*, 37: 427 (Jan.) 1918.
22. RANDALL, A., SMALL, J. C., and BIRK, W. P. *J. Urol.*, 5: 534 (June) 1921.
23. CASTELLANI, ALDO and MENDELSON, R. W. *J. Trop. Hyg. & Med.*, June 1929.
24. MCINTOSH, J. A. *Tennessee M. J.*, Nov. 1926; *J. A. M. A.*, 87: 996-1001, 1926.
25. PUND and GREENBLATT. *Arch. Path.*, 23: 224-229 (Feb.) 1937.
26. PUND and GOTCHER. *Surgery*, 3: 34 (Jan.) 1938.
27. D'AUNOY, R., and VON HAAM, E. *Am. J. Path.*, 14: 1 (Jan.) 1938.
28. GREENWOOD, F. G. *Brit. J. Radiol.*, 4: 488 (Oct.) 1931.
29. DESOUSA, ARANJO, and HERACLIDES CESAR. *Brazil Med.*, 29: 201, 1915.
30. GOLDZHIER and PECK. *Arch. Dermat. & Syph.*, 14: 14-27, 1926.
31. KAHLIL, M., NAMZI, M., PETER, F. M., SALAH H. DIN, M., and BELASHI, M. H. *Deutsche med. Wchnschr.*, 55: 1125 (July) 1929.
32. WILLIAMSON, T. V., ANDERSON, J. W., KIMBROUGH, R., and DODSON. *J. A. M. A.*, 100: 1671, 1933.
33. RAJAM, R. V. *Indian M. Gaz.*, 69: 372-375 (July) 1934.



# ANALYSIS OF FIFTY CASES OF PERFORATED PEPTIC ULCER\*†

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THIS study is based on a consecutive series of fifty cases of perforated peptic ulcer in which operations were performed in the seven year period from 1931 to 1937 at the Cumberland Hospital. Gastric as well as duodenal perforations are included, since the clinical picture and course are so similar that one may discuss both under the subject of perforated peptic ulcer. The operations on these patients were performed by a number of surgeons on the various surgical services of the hospital.

It is interesting to note that this group consisted entirely of males. In the past fifteen years, there has been no case of an operation for perforated peptic ulcer performed on a female patient at this hospital. One female patient was admitted, however, for recurrent ulcer symptoms and gave a history of a previous perforation for which she had been operated upon at another hospital.

There were six colored patients in this series, giving an incidence of 12 per cent, which corresponds to the percentage of colored patients admitted to this hospital.

The ages varied between 23 and 63 years, with an average age of 39 years. There were twenty-five perforations in patients between the ages of 35 and 50 years inclusive. (Chart 1.)

Twenty-seven cases of the total series occurred in the fall months, during September, October and November. (Chart II.)

Of forty-three cases in which an inquiry was made of symptoms suggestive of peptic ulcer prior to perforation, all but one gave such a history. The duration of these symptoms varied from one day to twenty-five years, with an average duration of three and one-half years. Eleven of these

patients had symptoms of one month's duration or less. A good number gave a history of an acute exacerbation of symptoms immediately prior to perforation. In three cases there had been positive x-ray findings of ulcer at some time prior to admission. Three patients had had a previous perforation, two, three, and seven years previously, respectively. Two cases perforated on the wards of the hospital, one five hours following a gastric analysis, and another during the course of observation for severe ulcer symptoms. (Chart III.)

Part of the diagnosis of a ruptured peptic ulcer therefore depends on eliciting a history of previous peptic ulcer symptoms, with an aggravation of these symptoms immediately prior to admission. All these patients experience a sudden, sharp, severe pain, located in the epigastrium (forty-two out of fifty), or occasionally around the umbilicus (six cases), or in the right lower quadrant (two cases). The pain then radiates to the right or left shoulder or both in a majority of cases (62 per cent), and occasionally to the right lower quadrant (in 21 per cent). Nausea and vomiting are infrequent symptoms. A history of the presence or absence of vomiting was elicited in thirty-nine cases. It was absent in twenty-one cases (or 42 per cent of the total) and, where present (in 36 per cent of the total), the patient gave a history of vomiting but once. The reason for this, is perhaps the "spill" of gastric and duodenal contents into the peritoneal cavity.

Abdominal muscular rigidity comes on immediately, and is "board-like" in character. This was noted over the entire abdomen in 64 per cent of the cases, limited to the right side in 14 per cent of the cases,

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† Presented at Brooklyn Day, American College of Surgeons Congress, October, 1938.

and limited to the upper abdomen in 22 per cent. It is interesting to note that most of the cases in which rigidity was limited to

appendicitis from ruptured duodenal ulcer. In our series an incorrect diagnosis of acute appendicitis was made in five cases. In all

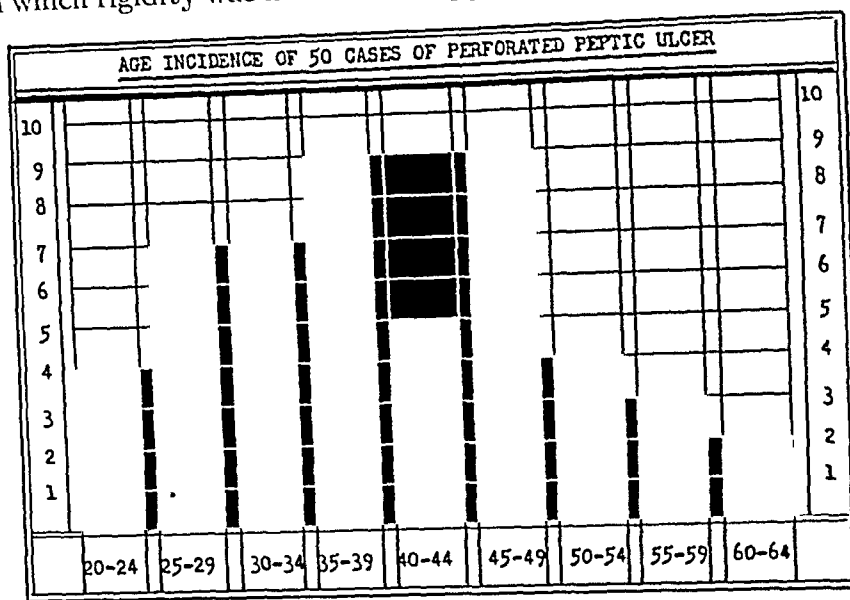


CHART 1.

the right side were ruptured duodenal ulcers, a helpful point in differentiating this type from ruptured gastric ulcers. The reason for this may be that the "spill" in ruptured duodenal ulcer is mainly along the right colic gutter. In a majority of cases, tenderness and rebound tenderness were elicited over the entire abdomen, with maximum tenderness in the epigastrium. In one-third of the cases of duodenal perforation the maximum tenderness and rebound were noted on the right side. This is important to remember in differentiating this condition from acute appendicitis. In twenty-six cases, the patient was examined for the presence or absence of liver dulness. Twenty, or 76 per cent, showed liver dulness to be partially or completely obliterated—a very important sign. The white blood count averaged 14,500, with 80 per cent polymorphonuclear cells. It was interesting to note that duodenal perforations gave a somewhat higher average (16,000) than gastric and pyloric perforations (13,000).

In considering the differential diagnosis of this condition, it is necessary to stress the importance of differentiating acute

these cases, the symptoms were found to be due to a perforated duodenal ulcer, making a 31 per cent error in the diagnosis of this condition. The reason for this incorrect diagnosis in ruptured duodenal ulcer is evident: the duodenal contents drain down the right colic gutter, causing a definite irritative chemical perityphilitis and peri-appendicitis, the symptoms of which mask the correct diagnosis.

Of the fifty cases, there were forty-eight in which the exact interval of time between perforation and operation could be determined. This varied between two hours and twenty-eight hours, with an average interval of seven hours. The average interval in those patients who survived was 5.93 hours, and in those who died 8.21 hours.

Of the twenty-nine patients who were operated upon within six hours, five died, a mortality of 17 per cent. Fifteen patients were operated upon within six to twelve hours from the time of perforation, and of these, five expired, a 33 per cent mortality. Of the two patients operated upon from twelve to eighteen hours afterward, one died, a 50 per cent mortality. One, operated upon at twenty-one hours, died. One



patient gave a history of having perforated twenty-eight hours before operation and survived. The history in this case, however,

tomy, was of the simplest character, performed in all but one case under general anesthesia. The operation consisted of the

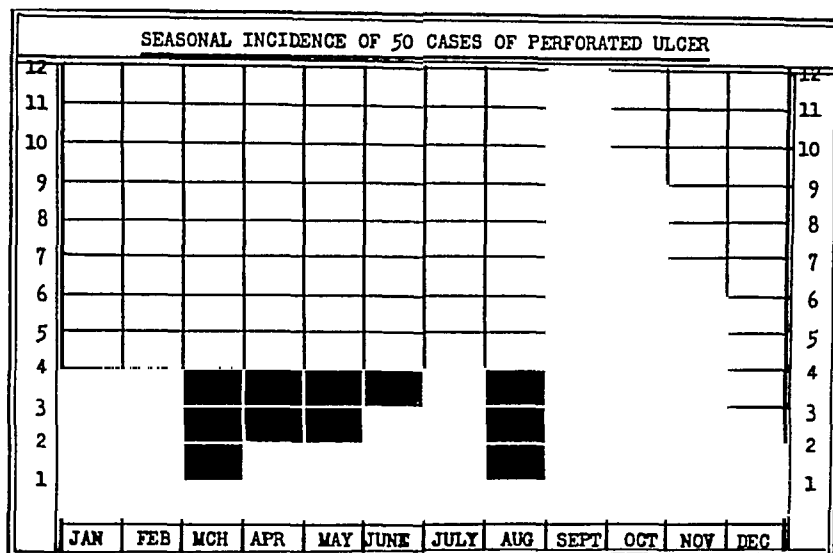


CHART II.

was obtained through an interpreter so that doubt may be cast on its veracity. As has been pointed out repeatedly by many writers, the mortality in these cases sharply rises as the time between perforation and operation increases. (Chart iv.)

The location of the perforation was determined at operation in all cases. All were on the anterior wall, and all within 2 inches of the pylorus on the gastric or duodenal sides. In twenty-seven cases, the perforations were on the gastric side, mostly near the lesser curvature; in seven directly at the pylorus, also near the lesser curvature; and in sixteen cases in the first portion of the duodenum.

The size of the perforation varied from a "pencil point" to 1 cm. in diameter. An area of induration was usually noted about the perforation varying from 1 to 5 cm. in diameter. The fluid present at the time of operation varied in quantity from 100 c.c. to 2,000 c.c. and also varied in color and consistency. It was generally noted that those who expired had a greater amount of fluid in the peritoneal cavity than those who survived.

The actual operation, with the exception of one patient who had a gastroenteros-

aspiration of the fluid, followed by a purse-string suture of the perforated area. This was reinforced with a continuous Lembert suture and then with a piece of omental graft. Drainage was instituted in a majority of cases. Forty-four of the fifty were drained by Penrose or rubber tube drains or both. Of these, ten expired, a mortality of 23 per cent. In six cases no drainage was instituted, and no deaths occurred. Only in very early cases, under twelve hours' from the time of perforation, was drainage not instituted. The average duration from perforation to operation in these cases was 5.2 hours. An attempt was made to determine the difference in the postoperative course of these drained and non-drained cases, but no conclusions could be reached because of the insufficient number of cases treated without drainage, and because of the occurrence of extra-abdominal complications in these cases.

Pulmonary complications occurred in ten cases, a 27 per cent incidence. This is extremely high. The question might be raised whether this might not have been lowered with spinal anesthesia. Wound infection occurred in six cases, uremia in two cases and phlebitis in one case.

An analysis was made of the factors related to the outcome of the cases and of the causes of death in each case, as discovered at autopsy. There were thirteen deaths, of which four were duodenal (out of sixteen) and nine were gastric (out of twenty-six), a mortality of 26 per cent. There were no deaths in the cases of perforation at the pylorus. (Chart v.)

The importance of the time factor between perforation and operation in determining the outcome has been mentioned. There was no appreciable difference in blood counts between those who died and those who survived. The size of the perforation had very little to do with the outcome, but generally those who died had a greater peritoneal "spill." Cultures of the peritoneal fluid were taken at the operating table on twenty-three cases. Of these, eleven were sterile, and twelve showed growths of pathogenic organisms either in pure or mixed cultures. Of the eleven cases in which the culture was sterile, three died, and of the twelve cases with positive cultures, one died. Thus, this factor has little influence on the mortality.

Six autopsies were done in the thirteen fatalities. Five died of generalized peritonitis and paralytic ileus. One patient with a four plus Wassermann, was found to have died of a bilateral bronchopneumonia and luetic aortitis. Of the five cases with generalized peritonitis, three were clinically declared to have expired from "shock"; they died six, thirty-one, and thirty-six hours postoperatively. One patient developed a bronchopneumonia, then eviscerated on the tenth day, at which time he was reoperated upon, and found to have a generalized peritonitis. He expired on the table. There was no autopsy in this case. Six proved cases of generalized peritonitis were therefore among the thirteen deaths.

Of the cases in which no autopsy was done, one died twenty-one hours postoperatively with a steadily mounting temperature—probably another case of fulminating peritonitis. It seems improbable that these seven cases of generalized

peritonitis, which account for 52 per cent of the total number of deaths, could have been saved by any procedure. The average

DURATION OF ULCER SYMPTOMS PERFORATION			
NO.	1 Month or less	1 Month to 1 year	More Than 1 year
18			
17			
16			
15			
14			
13			
12			
11			
10			
9			
8			
7			
6			
5			
4			
3			
2			
1			

CHART III.

interval between perforation and operation in these seven cases was seven hours.

One patient developed bronchopneumonia on the sixth day and died on the tenth day. One expired on the fifth postoperative day and was suspected of having a continued leak because of the difficulty in closing the perforation at the time of operation. He had a perforation  $\frac{1}{4}$  inch in diameter, surrounded by a large thick,

indurated area 1¼ inches in diameter. A futile attempt was made to purse-string this perforation, in the presence of edema-

fluid” noted, and the incision was extended upwards. On further observation, the intestines and omentum were found to be

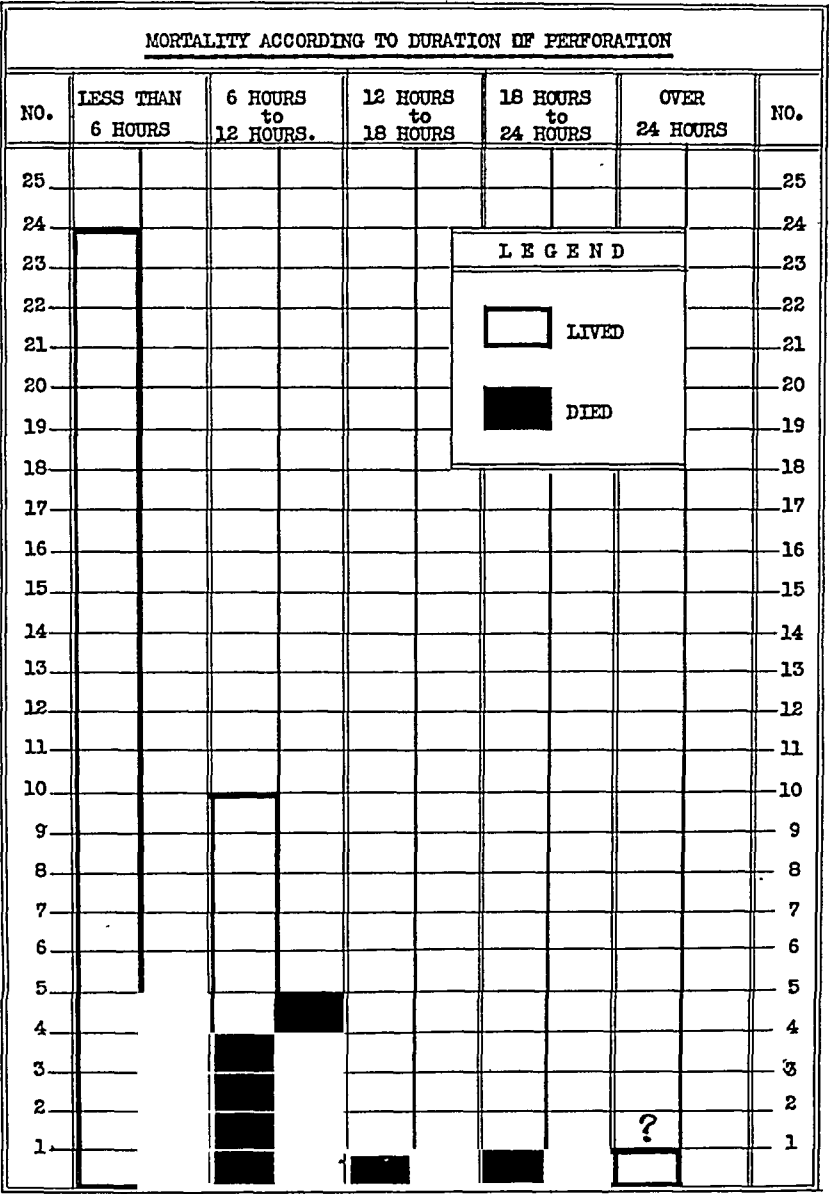


CHART IV.

tous friable tissue. This patient had a spill of 1,200 c.c. of fluid at the time of operation.

Three patients had developed shock during the operation, and never rallied subsequently. One of these gave a history of eight hours' duration from the time of perforation and was operated upon for acute appendicitis. The right lower quadrant was first explored, "considerable seropurulent

covered with a "white powder," taken at the onset of the symptoms of perforation. The total operating time was one hour and fifteen minutes. At the time the peritoneum was being closed, the patient's pulse suddenly became weak, and he expired two minutes thereafter on the operating table.

In the second case, the exact duration of the perforation could not be determined. The patient gave a history of vomiting and

epigastric pains for three days prior to admission, during which time he was probably having a subacute perforation. Two hours after admission, he suddenly complained of severe pain. He was immediately operated upon. His pulse was 130 per minute. He had a perforation 1 cm. in diameter, and another thinned out ulcerated area which "had almost perforated" in the middle of the lesser curvature, which was also purse-stringed. There were 200 c.c. of brownish fluid in the abdominal cavity. The total duration of the anesthesia was one hour and five minutes. During the operation, the patient's pulse became poor in quality. He was given intravenous fluids and he rallied somewhat. He expired, however, sixteen hours after operation in a state of shock.

The third patient was admitted and operated upon twenty-one hours after perforation, at which time he was moribund. His abdomen was markedly distended; he was cyanotic, dyspneic, and his pulse and blood pressure were unobtainable. The white blood count showed 3,100 white blood corpuscles. A "large perforation with a large amount of free fluid" was noted in the peritoneal cavity. He became progressively worse and expired nine hours postoperatively.

It is questionable if any of these cases would have been saved from shock and death by temporizing for several hours with preliminary shock treatment.

What happened to the thirty-seven patients who survived? Our follow-up concerns the twenty-seven cases followed. Of these, two died subsequently, one a year later of a gastric hemorrhage, and another nine months later following a posterior gastroenterostomy. Another patient was readmitted two and one half years later with severe gastric hemorrhage. He gave a history of having had two perforations which had been operated on and he was never free of symptoms. Seventeen patients, had no symptoms whatsoever, although four were still on a "diet." The remaining six patients, were fluoroscoped

three to four weeks postoperatively, and five failed to show any radiographic evidence of an ulcer.

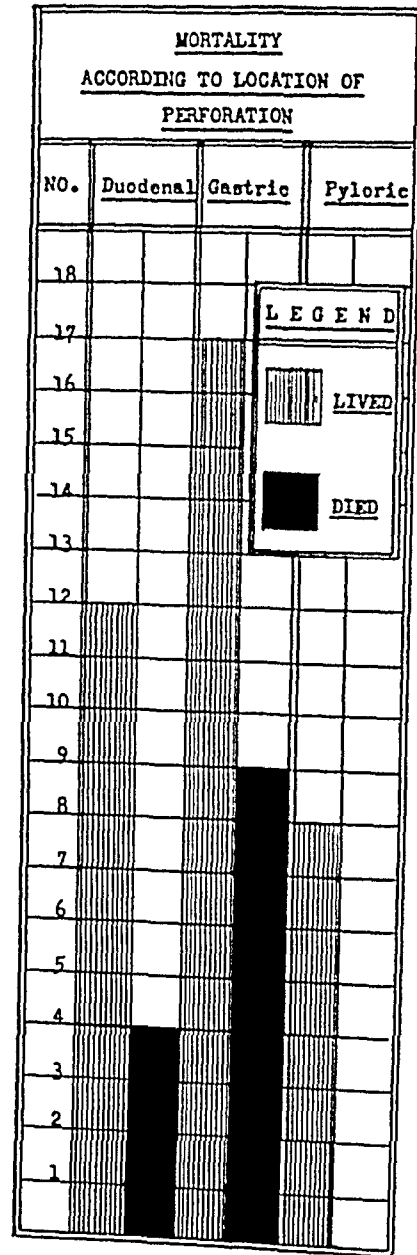


CHART V.

So one may say that, with the exception of the two patients readmitted for hemorrhage, most of the cases of ruptured ulcer were free of symptoms following their perforation.

#### SUMMARY

This study is based on a series of fifty cases of perforated peptic ulcer treated at the Cumberland Hospital during a seven

year period from 1931 to 1937. The average age of these fifty male patients was thirty-nine years. There appears to be a seasonal incidence for the occurrence of this condition. The majority of cases occurred in the fall months of September, October and November. Most of these patients had a definite history of peptic ulcer symptoms for an average duration of three and one-half years prior to perforation. The history of a sudden, sharp, severe abdominal pain followed by radiation of the pain to the shoulders appears important in the diagnosis of this condition. Objectively, the presence of marked abdominal tenderness, and rebound tenderness, with board-like rigidity of the abdominal muscles, and obliteration of liver dullness with a definite leucocytosis, make the diagnosis of the case

conclusive. The most important factor in determining the outcome is the interval of time between perforation and operation. The mortality rises sharply as this length of time increases. The simplest of operative procedures, namely, aspiration of the fluid and closure of the perforation, carried out with the least additional trauma is the procedure indicated. Generalized peritonitis appears to be the cause of death in a majority of the fatal cases. It appears unlikely that this may be influenced in any way, by delaying operation to improve the patient's condition, or by changing the operative procedure. A follow-up study of 73 per cent of the cases revealed that most of the patients were entirely free of symptoms, at an average of one and one-half years following the perforation.



# AN ANALYSIS OF THE CAUSE OF DIRECT HERNIAE FOLLOWING POSTOPERATIVE RECURRENCE OF INDIRECT HERNIAE\*

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THE treatment of lower abdominal wall herniae is still an intriguing subject, both in Europe and America. At the 1934 meeting of the British Medical Association,<sup>1</sup> Mr. Page stated: "In spite of all the consideration given to it, agreement about the best method of treatment has not been reached, largely because the information about late results is inadequate and inaccurate—a close follow-up would reveal a larger percentage of recurrences than generally believed." His own confidence in operations on all cases had been shaken by his experience with the Metropolitan Police. A review of 241 operations in that group disclosed the fact that 11.5 per cent were for postoperative recurrence, and further investigation suggested the true rate to be even higher.

Block's analysis of continental figures gave a recurrence rate of 34.8 per cent after two years, the majority apparently direct herniae.

T. A. Hindmarsh (Newcastle) reviewed 102 inguinal herniae with nine recurrences and stated that a large proportion of recurrences were due to the wrong type of operation, but did not state the reasons for his conclusions. His rate was slightly over 11 per cent. E. M. Cowell (Croyden) reported a recurrence rate of 4.5 per cent. Thus in the hands of capable English surgeons with the best modern technique, it was found that the recurrence rate was 4 to 11 per cent or higher, depending on the follow-up method employed.

A statistical report of 826 herniae (1933 to 1934) reported by O'Shea<sup>2</sup> shows 11.5 per cent recurrence. Burdich and Higinbotham,<sup>3</sup> advocating the radical proce-

dures of spermatic cord section in addition to other modern maneuvers to prevent recurrence, still had recurrences in simple herniae of 4.8 per cent, sliding 7.7 per cent, irreducible 6.5 per cent, and in postoperative cases a recurrence rate of 23.7 per cent.

Watson<sup>4</sup> makes the following observations and conclusions: (1) except for the rare traumatic type, all oblique herniae are congenital, regardless of age when first discovered; (2) congenital sacs in adults are more common than supposed and most men undoubtedly carry these potential sacs throughout life without incidence of herniae; (3) microscopic examination fails to show any difference between old and so-called new sacs.

Graham<sup>5</sup> states: "The congenital origin of most inguinal hernial sacs has been almost universally accepted for twenty-five years in this country, having been recognized by nearly all Workmen's Compensation Boards, who take the position that there is a distinction between a potential and an actual hernia—that it is an accident or injury of some kind that transforms the potential into the actual hernia. Even if a man has a congenital sac, but without the actual hernia, he is unconscious of the condition and can hardly be said to have a hernia, until there is a protrusion of omentum or viscus."

Thus in a review of the literature on the subject of direct and indirect herniae, one finds the following:

1. Many data covering varied types of operation and maneuvers for the purpose of avoiding recurrence.

\* From the Daniel Baugh Institute of Anatomy, Jefferson Medical College of Philadelphia.

2. A general agreement in the statement that inguinal herniae have a congenital basis, with discussion pro and con upon the subject, as to what value should be given to the non-obiterated peritoneal sac or funnel as an actual cause of hernia formation.

3. A fairly uniform percentage of recurrence after operation when done by the best surgeons, with the most modern technique in both England and America. Also the surprising fact that the percentage of recurrences after operation for operative failure jumps from 11.5 per cent to 23 per cent.

In spite of all the discussion, both written and oral, upon the subject of hernia, the problem seems to be of as much interest and importance today as it was fifty years ago.

The material found in the literature brings certain fundamental questions to our attention, such as: (1) Why should the majority of recurrences be direct herniae when the original operations were for indirect herniae? (2) What is the important factor in hernia formation if the sac of peritoneum, intra-abdominal pressure or the viscus is not the primary cause of hernia?

In an endeavor to solve these questions, the thought occurred that in the original concept of hernia formation the effect rather than the cause was considered. A concept of effect naturally produced a tremendous interest in methods of repair and reconstruction, and resulted in innumerable maneuvers and modifications of surgical technique, none of which is universally successful in avoiding operative recurrence.

Many investigations have clearly shown that hernia is not caused by intra-abdominal pressure, nor by the presence of a congenital sac of peritoneum, nor by the protruding viscus, alone or in combination, and that in the majority of individuals, direct and indirect herniae will not develop unless the anterior abdominal wall muscles are torn, as in trauma. These facts led to the conclusion that there must be some

other fundamental factor or factors which have not as yet received proper attention.

Study of the subject resulted in a description of an average anatomic type or pattern, and variations from the average type.<sup>6,7</sup> The latter I believe to be the important factor underlying hernia formation, i.e., the protrusion of a viscus. These muscle variations constitute an inherent weakness of construction in the anterior abdominal wall. They are caused by deviations in the embryonic development of the musculature and result in variations of pressure resisting efficiency. It can be demonstrated that in the presence of a viscus protrusion or hernia there is an almost constant finding of a variation from the average anatomic muscle picture.

For the purpose of this paper, I shall describe and discuss the average anatomic pattern and variations from the average anatomic type which I believe to be the fundamental cause of hernia formation, and shall attempt a rational explanation for the occurrence of direct hernia as a postoperative sequela of indirect inguinal herniorrhaphy, as well as suggestions leading to the general problem of inefficient anterior abdominal walls when due to variations in the musculature.

An average pattern of the anterior abdominal wall may be described as follows: It is a flat musculofascial structure consisting of two plates on either side of, and fused at the midline (linea alba). Each plate is composed of three laminated superimposed muscles of which the external oblique is passive and the internal oblique and transversalis muscles are active in hernia prevention, and therefore will be the muscles considered. Each musculofascial plate may be divided into two major divisions, a medial and a lateral, united by a curved fascial condensation or reinforcement—the linea semilunaris. The latter is the lateral demarcation of the rectus abdominis sheath and extends from the costal margin to the lateral aspect of the pubic bone. Each division is partly muscular and partly fascial or aponeurotic with a

maximum of muscle and a minimum of fascia. Muscle arches, consisting of superimposed internal oblique and transversalis muscle fibers, are found in the caudal part of each division. From the concave edge of these muscle arches attenuated fasciae are prolonged to attachment on the coxal bone and inguinal ligament, these are the result of the transformation of muscle into fascia due to growth tension of the laminated superimposed muscles. The medial pillars of these two arches seemingly fuse with the caudal extremity of the fascial reinforcement (the linea semilunaris) to form a musculoaponeurotic structure, the conjoined tendon, for insertion into the lateral aspect of the pubic bone. The lateral pillars of the arches are inserted respectively into the inguinal ligament (iliopubic line), to the midline (symphysis pubis), and buttressed by an intermediate pier of support at the lateral aspect of the pubic bone, the conjoined tendon. Filling the areas of attenuated fasciae are inserted laterally the spermatic funiculus and medially the rectus abdominis muscle. The arches of muscle are of such size that a minimal muscular contraction will cause the fibers of the muscles (internal oblique and transversalis) to hug the inserted structures and obliterate the arch areas. It now becomes evident why an elastic, muscular anterior abdominal wall, which by its own minimal contraction obliterates the seeming openings, can so successfully oppose intra-abdominal pressure and make viscus protrusion improbable, if not impossible.

Variations of the average pattern may be found in each component of the abdominal wall; these variations influence the coördination of its component parts and their potentiality for hernia prevention. The reasons for the small number of herniae generally found where the areas of muscular deficiency are greater than average, is the presence of a minimal degree of variation in other components of the wall. This and the ability to effect a shift or coördinated interplay of the whole wall, result in

the interposition or substitution of one muscular part for another.

Variations of the average anatomic pattern may be found as recessions of all degrees—from the absence of recession (where due to defective tension lines the muscle failed to recede from the inguinal ligament and pubic bone, and to form arches) to recession of such magnitude that the arches almost reach the level of the umbilicus, in the medial divisions, and 1.5 inches above the anterior-superior spine, in the lateral divisions of the abdominal plates, thus making evident the fact that all musculature of the lower anterior wall has been transformed into attenuated fascia. This condition may occur in one or both of the superimposed internal oblique and transversalis muscles and their conjoined tendon component, resulting in either a completely muscular anterior abdominal wall where there is absence of recession, or an anterior abdominal wall (the internal oblique and transversalis muscles) that contains a minimum of muscle fibers and a maximum of fascia with large inelastic arches in its caudal aspect.

While such variations may occur in the abdominal wall, when considered as a unit of two superimposed muscles, they are also found in each component of the internal oblique and transversalis muscles, being present as a variant in one muscle or its parts with average pattern in the other. It should also be noted that the conjoined tendon, being a part of the muscles, will be influenced by the factors affecting the muscles and will, therefore, show all degrees of variation from a maximal muscular to a minimal muscular or fascial structure. The rectus abdominis muscle, being a part of the flat abdominal wall, although a distinct developmental entity, will be influenced by the same growth mechanism that affects the internal oblique and transversalis muscles and will, therefore, show the same types of variation. The lower part of the rectus abdominis muscle, due to the strain, will be muscular or



fascial to a greater or less degree, depending on the stress put upon its musculature after completion of contact with the pubic bone (14 mm., 7-8 week embryo), and will be manifested as short, bulky, muscular and long, attenuated and tendinous insertions.

These insertions, located in areas of attenuation of the anterior abdominal wall that are greater than average, will influence the potentiality for hernia in direct proportion to the amount of muscle or fascial content found in the insertion, and will affect its ability to substitute for the absence of musculature in the areas of deficiency of the abdominal wall plate. The more muscle fibers present in the lower rectus abdominis muscle, the greater its ability to contract and increase its diameter, the more effective it becomes as an aid to the protective mechanism of the anterior abdominal wall required in resisting intra-abdominal pressure and hernia formation.

From the foregoing, it becomes apparent that herniation or viscus protrusion is primarily dependent on the variations of the average pattern and upon distortion of the tension lines of the anterior abdominal wall. The amount of variation may be divided arbitrarily into three groups for the purpose of discussion. The variations range from 1 per cent to that degree of maximal variation where there is entire absence of muscle fibers in the anterior abdominal wall below the umbilicus, which may be considered to be 100 per cent variation.

In group A belong those cases which may be considered as being concerned mainly with failure of the pressure-resisting function of the anterior abdominal wall. An efficient pressure-resisting body wall is one in which, though there be present any degree of structural variation in its component parts, acts so efficiently in the usual routine activity of the individual, that it is able to coördinate them into a unit of 100 per cent competency in resisting intra-abdominal pressure and preventing protrusion of a viscus. In these cases hernia may not occur, except in the presence of certain conditions that impair efficiency

and act simultaneously. These certain conditions are (1) a flexed trunk which relaxes the abdominal wall musculature and makes maximum contraction impossible; (2) sudden increase in intra-abdominal pressure; and (3) the aid given by the presence of a peritoneal sac. In the modus operandi of hernia formation, the intra-abdominal pressure forces a viscus to push aside the inefficiently contracted muscle and to appear externally as a protrusion or hernia. The above may be considered as applying to both the congenital and the acquired types of viscus protrusion.

In the so-called congenital type, the partially or wholly unobliterated peritoneal sac only influences the rapidity and extent of the protrusion beyond the anterior abdominal wall. In the acquired type, the formation of the sac is governed by a continuous operation of factors of strain with only the inherent inelasticity of the peritoneum to oppose it.

The treatment of this group where the musculature is generally efficient with only occasional lapses of efficiency, is simple reduction by taxis, rest in bed to allow the stretched and traumatized muscles to recover from the unusual stretching of the fibers, to be followed by muscle training, such as gymnastics. Individuals of this group may continue throughout life without a repetition of the primary occurrence. Industry recognized this group many years ago and provided loading platforms for its burden carriers. This group does not need routine operative interference, except in the acquired type, in which type, injection, or any nondistorting operation is effective as a cure. This group has no recurrences, except those due to infection or improper suturing. Recurrences are generally indirect inguinal herniae, except where the suturing causes marked distortion of the conjoined tendon and enlargement of the middle arch, in which case the recurrences will appear as direct herniae.

In group B belong those cases in which the musculature is of such degree of variation that even in maximum contraction of

the anterior abdominal wall there is no obliteration of the deficiency arches of the internal oblique and transversalis muscles, and in which the structures may not be reconstructed without an amount of distortion of the conjoined tendon, thus impairing the maintenance of the lines of tension of the abdominal musculature. It is in this group that recurrences generally occur in the middle arch, as direct herniae, because changes in position of the conjoined tendon, relative to the other component parts of the abdominal wall result in the enlargement of the middle arch, and greater functional and structural inefficiency of the anterior abdominal wall.

In group c belong those cases which have very little or no muscular fibers in the anterior abdominal wall below the level of a line drawn between the anterior superior spines. Attempting to repair this group without anatomic structures other than those of the abdominal wall, will distort the conjoined tendon and give recurrence in the middle arch—direct herniae. In this group the percentage of recurrences will approximate 100 per cent irrespective of any maneuvers made. Use of fascial flaps with some external support, such as a belt, may prove partially successful.

I have refrained from recommending any specific surgical procedure because it is my belief that further study will develop criteria of evaluation of the various types and will lead to specific treatment for each anatomic type. Routine injection treatment I believe to be a transient fad rather than a constructive maneuver for prevention of herniae, because it fails to consider the very evident fact that scar tissue can never replace elastic muscle in the function of pressure resistance. An adequate and accurate follow-up over a period of time will either cause it to be discarded or limit its use to a very small group of selected cases of the A group of anatomic variations.

I wish to extend thanks to Dr. J. Parsons Schaeffer, Director of the Daniel Baugh Institute of the Jefferson Medical College for his interest and helpful suggestions in the preparation of this paper.

#### REFERENCES

1. PAGE, M. *Lancet*, 2: (Sept. 8) 1934.
2. O'SHEA, M. C. *New York State J. Med.*, 35: 473-470 (May 1) 1935.
3. BURDICH, C. G., and HIGINBOTHAM, H. L. *Ann. Surg.*, 102: 863-874 (Nov.) 1935.
4. WATSON, L. F. *M. Rec.*, 139: 323 (April 4) 1934.
5. GRAHAM, EVARTS. *Year Book of Surgery*, 1935.
6. CHERNER, M. *Ann. Surg.*, 99: 577-584 (April) 1934.
7. CHERNER, M. *Am. J. Surg.*, 44: 593, 1930.



# TRANSURETHRAL RESECTION FOR CANCER OF THE PROSTATE\*

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## INTRODUCTION

THE dire outlook and frequent occurrence of cancer of the prostate make it an unhappy topic for discussion. There are several reasons for the poor prognosis. The tumor itself causes no symptoms; they are due to encroachment upon the urethra, to extension into adjacent structures, or to metastasis. Because the cancer usually grows slowly, symptoms appear late in its course. Chwalla had two patients who lived seven and eight years respectively after cystostomy.

Two other factors operate to defer the onset of obstruction to urination; slow growth of the tumor permits the detrusor to hypertrophy and to compensate for the obstruction until it is quite advanced; and carcinoma of the prostate usually arises in the posterior lobe of the gland, at a relatively great distance from the urethral lumen. (Moore found that 73.7 per cent originated in the posterior, 14.8 in the lateral, and 8.8 in the anterior lobes. None had their origin in the median lobe.) Moreover, the symptoms of carcinoma of the prostate have the same age incidence as and at first are indistinguishable from those of benign hypertrophy; patients are likely to regard them as the inevitable accompaniment of advancing years and to ignore them until they become intolerable or until pain from metastasis appears. They are therefore likely to consult the physician late.

Because of the slow growth of the tumor, the late appearance of difficult urination, and procrastination by the patient, local extension and metastasis are likely to be found when he is first examined. Thus Barringer found the tumor apparently

confined within the prostatic capsule in but fourteen of 351 cases (4.5 per cent), and Colston has stated that Young found but thirty-six of 1,040 cases (3.4 per cent) suited for radical operation.

Moreover, clinical evidence of metastasis to bone was found by Ferguson in 30 per cent of his cases, and by Bumpus in 24.3 per cent of those patients in whom x-rays were made when they were first seen. Also, Ferguson discovered perineural cancerous infiltrations in 52 per cent of patients coming to autopsy; Graves, Warren, and Harris found them in all.

## INCIDENCE

The problem is made more serious by the frequency of the disease. It is variously estimated as causing: 20 per cent of all obstructive lesions of the prostate (Young); 0.6 per cent of all deaths, and 4 per cent of all cancer deaths in the male (Caulk). Prostatic carcinoma was found in 14 per cent of 292 consecutive autopsies in the male by Rich; in 21 per cent of all autopsies on males past 41 by Moore; and in 23 per cent of necropsies on patients past 70 by Muir.

From these figures the seriousness of the problem is apparent. Young has stated that the disease is on the increase, and Duff found that the death rate from carcinoma of the prostate among the male industrial policyholders of the Metropolitan Life Insurance Company increased from 0.8 per 100,000 in 1917 to 3.7 per 100,000 in 1928. It is not clear whether this is a real increase or an apparent one due to the recent increase in longevity, as well as to the change in attitude toward lesions of the prostate evoked by the development of transurethral resection. In connection with the

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former hypothesis, it is worth noting that the life expectancy from birth of the group of Metropolitan policyholders mentioned above increased from 46.6 years to 60.7 years between 1911 and 1937. This increase in individuals living in the higher age brackets is undoubtedly responsible for a large part of the apparent increase in cancer.

Moreover, the development of resection is also an important factor because it has led to a great increase in the number of patients submitting to operation and has produced an apparent but artificial increase in the incidence of all forms of prostatic obstruction.

#### DIAGNOSIS

The symptoms of carcinoma are those of any obstructive lesion at the vesical neck until local extension or metastases appear. Prior to that time the diagnosis is made by rectal palpation. When the gland is nodular, stony hard, and fixed, this is simple. When the carcinoma is still an isolated, movable, hard nodule (and this is the only time when there appears to be any chance of cure) definite identification of the nodule as cancer is difficult, and biopsy is indicated. The simplest method is that of aspiration through a needle inserted via the perineum. While Keyes and Ferguson have secured positive diagnoses by this method in 86 per cent, its satisfactory use requires a pathologist with considerable experience in making diagnoses from minute fragments of tissue. The percentage of accuracy in most hands will probably fall far below that level.

Tissue may also be secured with the prostatic punch or resectoscope, but this method is least useful when most needed, i.e., in the presence of a small nodule in the posterior lobe, when even an extensive resection will yield only the benign tissue which lies between the lumen of the urethra and the nodule.

The presence of osteoblastic metastases in bone is diagnostic, but of hopeless

import; the same is true of the presence of metastatic cancer in removed lymph nodes.

With all these measures available, the incidence of error ought to be low in the hands of the careful observer, especially if routine sections are made of all material removed at operation in order to detect the occasional carcinoma which cannot be palpated because it is surrounded by benign hypertrophy.

#### TREATMENT

As is evident from the discussion of prognosis, treatment is usually ineffective as far as cure is concerned. Factors already discussed usually postpone the discovery of cancer of the prostate until too late for complete removal. Nevertheless, a good deal in the way of palliation can be accomplished by thoughtful treatment. The methods in general use may be classified as follows:

##### A. Curative:

1. Radical prostatectomy.
2. Conservative prostatectomy (enucleation of "concealed" cancer).

##### B. Palliative:

1. Diversion of the urine.
2. Surgical removal of the obstructing tissue.
3. Irradiation.
4. Combinations.

Radical prostatectomy is the only method which offers any hope of cure. While Marion has performed the operation suprapubically, the greater risk inherent in this exposure and the practical impossibility of exposing the posterior surface of the prostate for biopsy, make the perineal approach much more satisfactory. Radical perineal prostatectomy, despite a mortality of 11 per cent and considerable risk of incontinence, offers the chief hope of cure in prostatic cancer. Unfortunately, the low rate of operability (3.43 per cent in Colston-Young's series) makes the operation inapplicable to most cases. While Young has had 50 per cent of five-year cures and freedom from recurrent obstruction in the remainder, this 3.43 per cent operability

reduces the percentage of cures from 50 per cent of operable cases to 1.71 per cent of all cases, a situation remediable only by earlier diagnosis. Smith has had essentially the same results as Young.

Enucleation of a cancer concealed and localized within a spheroid of benign hypertrophy has been enthusiastically proclaimed of late by the opponents of transurethral resection. They declare that the widespread use of the latter has deprived many patients of their chance of cure—a serious indictment of the transurethral operation until one considers all the facts. Only about 8 per cent of cancers of the prostate (twenty-seven of 325 cases of von Illyes), or about 1.6 per cent of obstructive lesions at the vesical neck are concealed within spheroids of benign hypertrophy. In ninety-six cases of concealed cancer assembled from reports by Cunningham, Hirsch and Schmidt, von Illyes, and Bugbee there were twenty-five (26 per cent) of two to five-year cures. Setting the incidence of concealed cancer at 1.6 per cent of all obstructions at the vesical neck, this means that complete replacement of enucleation of the prostate by transurethral resection would lead to the loss of an opportunity for cure of concealed cancer in  $\frac{4}{10}$  of 1 per cent ( $0.26 \times 0.016$ ) of the patients—a loss far outweighed by the lower operative mortality of the transurethral operation.

Diversion of the urine is unsatisfactory. Catheterization leads to an infected, irritable bladder which makes the passage of the catheter painful and requires it frequently. Inlying catheters are notoriously difficult to manage without continuous, expert supervision. Suprapubic cystostomy is more comfortable, but the necessary apparatus causes a great deal of inconvenience and requires special care. Bumpus in 1924 found that the postoperative life averaged twenty-four months with 5 per cent of five-year survivals.

Irradiation is admittedly palliative. High voltage x-ray is of value chiefly in relieving pain and in augmenting the effect of radium

or radon. Dolan has recently canvassed sixty-three urologists concerning cancer of the prostate; none of them had had a ten-year cure from irradiation; several had had five-year cures; Caulk has never seen a cure, and Barringer estimates that about 10 per cent of prostatic cancers can be controlled for five or more years by a combination of interstitial irradiation (radon) with high voltage x-ray therapy.

Transurethral resection is too recent in development to permit an accurate determination of end results, although many discussions of the operation refer with satisfaction to its use in prostatic cancer. Stirling canvassed sixty urologists in 1934 and found that forty-two favored the application of the operation, with or without supplementary irradiation, to cancer, while twelve favored radical perineal prostatectomy but deplored its infrequent applicability.

Bugbee has reported fifty-two cases of prostatic cancer treated by transurethral resection without an operative death. Nine had died of cancer and three from heart disease from twelve to forty-four months after operation, and forty were living from one to forty-eight months with satisfactory micturition. Three had required reoperation.

Jacobs used the operation in fifteen cases with one operative death. Four had died of cancer from three to twenty months after operation, three were not relieved and required cystostomy, and seven were living without obstruction for one to thirty-three months.

Caulk was able to follow 129 cases treated with his cautery punch. Obstruction was relieved in 77 per cent. In 30 per cent life continued three years, 18 per cent four years, 5 per cent seven years, and one patient was living fifteen years with signs of cancer.

Thompson and Emmett have reported the results of the punch operation in 107 cases of prostatic carcinoma. There was one operative death (0.9 per cent). Twenty-four patients died during the first year following

operation, and twenty-seven more during the ensuing ten years. Eleven required reoperation for recurrent obstruction after varying intervals, and fifty-six were living after six to forty-eight months.

#### CASE REPORTS

The material consists of all cases of carcinoma of the prostate treated by transurethral resection at the University Hospital, Minneapolis from April, 1930 to December 31, 1936. At least one year had elapsed following operation in the last case when this study was begun.

During this period the diagnosis of carcinoma of the prostate was made 275 times. One hundred two patients were treated by transurethral resection with or without supplementary irradiation with interstitial radon and x-ray; 112 received irradiation only, twenty-nine had prostatectomy,\* of whom twenty-two were also irradiated; eleven had cystostomy,\* of whom eight were irradiated; three had radical perineal prostatectomy; and eighteen, were, for a variety of reasons, not treated at all.

Thus transurethral resection was employed in 37.1 per cent of the cases in which the diagnosis of cancer was made. It was used only in the presence of troublesome obstruction to urination. The average age of the patients was 69.6 years; the average residual urine was 440 c.c., and the average amount of tissue removed was 13.1 Gm., the extremes being 1 and 66 Gm. The operative mortality was 1.9 per cent. Demonstrable metastases to bone were visible in 19.6 per cent of the patients when first seen, the lumbar spine and pelvis having been x-rayed in all.

It was intended in all cases to relieve the obstruction with the Stern-McCarthy resectoscope, and six weeks later to irradiate the prostate. In approximately half the cases irradiated, radon was inserted

\*The forty cases treated by partial prostatectomy and by cystostomy were encountered early in the series before the writer felt that he had developed sufficient facility with the resectoscope to permit him to attack larger prostates with it.

through the intact perineum into the prostate and was followed at once by a course of high voltage x-ray therapy by a modification of Coutard's method. In the other half of those irradiated the x-ray therapy was started six weeks after the operation and radon was implanted at its conclusion. The average dose of radon employed was 30 millicuries in gold implants with walls 0.3 mm. thick and containing 1 to 2 millicuries each.

The object of allowing six weeks to elapse between operation and irradiation was to obviate the untoward reactions which followed simultaneous operation and implantation of radon in my early experience.

Thus it was intended to treat all of this group of 102 patients by the same method, i.e., there was no deliberate selection of one patient for transurethral resection alone, another for operation plus radon, etc. However, thirty-five patients failed to return for irradiation, fourteen came back for radon but not for x-ray; nine returned for x-ray but not for radon; and forty-four had both. There is thus an opportunity, limited by the small size of each series, to compare operation alone with operation plus radon, plus x-ray, and plus both, without the factor of deliberate selection of the patient for a given type of treatment.

The only pleasing features about the results were the low operative mortality (1.9 per cent) and the high percentage of patients relieved of obstruction. In only three patients (3.0 per cent) of those surviving operation was it found impossible to relieve the obstruction to urination by transurethral resection. All three were seen in 1930 and 1931. In two more, naturally not included in the series, resection was thought advisable but could not be done because the instrument could not be inserted.

In one patient the obstruction recurred and was not relieved despite another resection. Cystostomy then had to be done. In another, obstruction recurred but the resectoscope could not be inserted, so that cystostomy was necessary.

In five patients recurrent obstruction necessitated re-resection, which again yielded relief. The shortest interval between opera-

A lower mortality is a powerful argument for any palliative operation. Colston has reported 250 partial perineal prostatec-

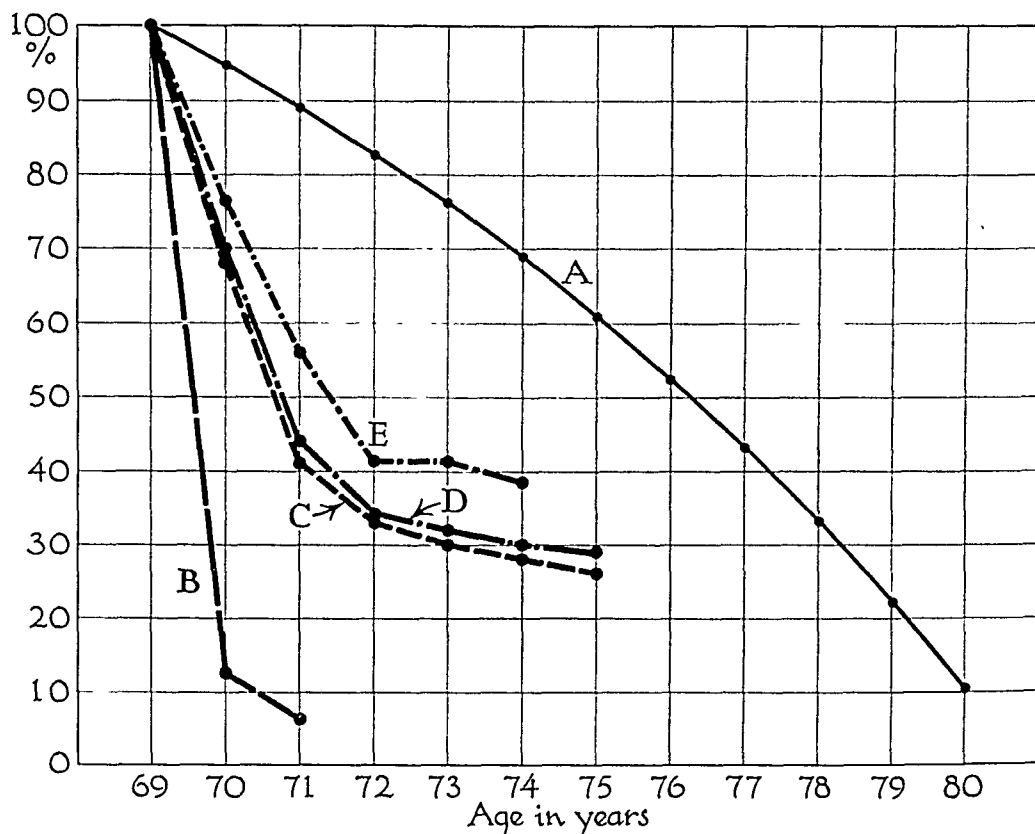


FIG. 1. Survival after treatment of prostatic carcinoma. A, expected survival in male population. B, survival of untreated carcinoma of prostate. C, survival after transurethral resection followed by irradiation. D, survival after transurethral resection with and without irradiation (whole group). E, survival after transurethral resection alone.

tions in this group was four months; the longest thirty months. One of these patients was operated upon first in 1931 and again in 1932 and 1934 for recurrent obstruction.

The operation achieves the same results as partial prostatectomy or the enucleation of a coexisting benign hypertrophy with a shorter hospital stay and a lower risk. Prostatectomy involves an average stay of fourteen days before and thirty days after operation (Swan and Mintz); that for resection is much shorter; Thompson has been able to omit preoperative drainage entirely in 60 per cent; the total hospital stay from admission to discharge for out of town residents in my experience averaged seventeen days in 400 resections.

tomies for cancer with an operative mortality of 6.9 per cent which is probably far lower than that of partial suprapubic prostatectomy. One can probably anticipate a mortality of less than 2 per cent from transurethral resection (below 1 per cent—Thompson, Caulk).

Moreover, the end results do not appear to favor partial prostatectomy, since Colston found the average postoperative survival to be twenty-five and Bumpus thirty months after the perineal and suprapubic operations, respectively. However, there are not yet enough data available to ascertain the average survival after resection. Its lower mortality, shorter hospitalization, and reduced discomfort doubtless leads to its application to much poorer

risks and may thus shorten the average postoperative survival.

### RESULTS

As may be seen from Table 1, of the thirty-five patients treated by transurethral resection, the thirty-four who were followed had an average postoperative life of twenty months, including the ten (29.5 per cent) still living after an average of 33.09 months; all seven of those requiring reoperation were in this group.

Among the ten survivors, six, or 60 per cent, were symptom-free from eighteen to sixty-five months. The remaining four have nocturia varying from three to eight times without symptoms of obstruction, from sixteen to seventy-three months after operation.

The thirteen followed patients of the fourteen treated by resection and interstitial radon lived an average of 16.5 months, including the four (30.8 per cent) still living an average of 34.7 months. Of the four survivors, one (25 per cent) has been well twenty-six months. Of the remaining three, one complains of frequency without obstruction at sixteen months, and two have nocturia three times with slight straining at thirty-nine and fifty-eight months.

Of the nine receiving resection and x-ray therapy, the eight followed patients lived an average of 16.5 months, including the two survivors who are living thirty-one and thirty-four months. One has nocturia three times without obstruction at thirty-one months, and the other is moribund with pain but without retention at thirty-four months.

In the forty-four receiving resection, radon and x-ray, there was an average survival among the forty-two followed of 20.4 months, including the six (14.5 per cent) still living an average of 36.2 months. Of these, two (33 per cent) are well twenty-two and thirty-two months after operation. Of the remaining three, two have nocturia six to eight times; the other is troubled by straining.

Figure 1 shows the comparative effect of the various types of treatment upon the mortality of the patients in terms of the percentage dying during each successive year following treatment. The top line represents the expected deaths in the male population of the United States (Dublin and Lotka). The bottom line represents a group of eighteen untreated patients. It may be seen that mortality of the disease is reduced by treatment, and that the addition of irradiation to transurethral resection had no very significant influence upon mortality. It should be remembered that the curve makes no allowance for the reduced rate of recurrent obstruction which follows irradiation, nor for the additional comfort conferred upon those with pain.

Thus if it is permissible to draw conclusions from such small groups of cases, one may say that urinary retention from prostatic carcinoma can be relieved in 97.1 per cent by transurethral resection; the duration of life thereafter is not materially increased by postoperative irradiation with radon, with x-ray, or with both. The tendency for obstruction to recur is lessened by irradiation, but the highest percentage of symptom-free survivors follows operation not supplemented by irradiation. It should be noted, however, that x-ray therapy has proved most effective in relieving temporarily the pain from perineural infiltration and from metastases to bone, and is therefore more than justified. The tendency of irradiation to cause shrinkage of the prostate when used alone deserves mention, but will not be discussed.

It has been alleged that transurethral resection is unsurgical in that it cuts through cancer without attempting to cure, and that the cut cancerous surface will not heal. These statements are doubtless true; this is of small moment when one considers the gain in comfort without dependence upon apparatus which is thus secured at a relatively small cost in terms of risk and expense.

It is also stated that transurethral resection causes metastases by traumatizing



cancerous tissue. This is probably untrue. Bumpus observed an average postoperative survival of twenty-four months following cystostomy, while the average postoperative survival for this series is 19.45 months, including those still living. This must be modified by the fact that the survival after the onset of symptoms in Bumpus' series was fifty-seven months; in this group it was 56.57 months. In other words, Bumpus' series of 117 cases was composed of private patients who sought treatment earlier and were treated by a method which did not traumatize the cancer itself; their disease ran its course in

26 per cent of two to five-year cures, but correction of these figures for incidence and operability changes the figure to 2 per cent of all prostatic cancers. The rate of five-year survival by transurethral resection is yet to be established; the fact that 24.8 per cent of the followed cases in the writer's series are living an average of thirty-four months suggests that the results will compare favorably with those of the methods mentioned above.

#### SUMMARY AND CONCLUSIONS

1. A series of 102 cases is presented in which carcinoma of the prostate was

TABLE I  
RESULTS OF TRANSURETHRAL RESECTION

Treatment	Number of Cases		Bone Metastases on Admission	Operative Deaths	Average Survival (Dead)			Average Survival (Living)			Average Survival (All)
	Total	Followed			No.	Per Cent	Length of Life (Months)	No.	Per Cent	Length of Life (Months)	Length of Life (Months)
Resection	35	34	6	2	24	70.5	13.5	10	29.5	33.09	20.23
Resection, radon.	14	13	7	0	9	69.2	7.78	4	30.8	34.74	16.53
Resection, x-ray	9	8	2	0	6	75.0	11.29	2	25.0	32.5	16.59
Resection, radon and x-ray	44	42	5	0	36	85.5	18.3	6	14.5	36.2	20.48
Total	102	97 (95%)	20 (19.6%)	2 (1.9%)	73	75.2	13.5	22	24.8	34.18	19.45

Percentages, except of operative mortality, are based on cases followed.

fifty-seven months after the onset of symptoms. This series is composed of 102 charity patients who received treatment later by a method which did traumatize the cancer; their disease ran its course in 56.5 months after the onset of symptoms. Therefore one may assume that transurethral resection of the cancerous prostate does not provoke early and widespread metastases.

Even if it did, it is not clear that this would contraindicate its use; radical perineal prostatectomy yields but 1.7 per cent of five-year cures when the results are corrected for the percentage of operability; enucleation of concealed cancer yields

treated by transurethral resection, supplemented by irradiation with radon in fourteen instances, with x-ray therapy in nine, and with both in forty-four cases.

2. There were two operative deaths (1.9 per cent).

3. Obstruction to urination was relieved in ninety-nine (97 per cent).

4. Recurrent obstruction required reoperation in seven (6.8 per cent), all in the group treated by resection alone.

5. The average duration of life was 56.5 months after the onset of symptoms, and 19.45 months after treatment, including twenty-one patients (24.8 per cent) still living after an average of 34.18 months.

6. Of the twenty-one survivors, nine (9.2 per cent of those followed) are symptom-free after 29.6 months; twelve (12.3 per cent of those followed) have moderate frequency of urination after 37.6 months; three of these have evidence of recurrent obstruction not severe enough to require treatment. That is, 21.5 per cent are living and at least tolerably comfortable three years after operation.

7. The longest symptom-free survival is sixty-five months; the longest survival with symptoms is seventy-three months (both after resection without irradiation).

8. The vast majority of those who died did not suffer from recurrent obstruction.

9. Transurethral resection affords a safe method of relieving the obstruction to urination from carcinoma of the prostate. It offers no prospect of cure, but is a more comfortable substitute for catheterization or cystostomy, and a safer substitute for partial prostatectomy.

10. Irradiation with interstitial radon and x-ray does little but reduce the tendency to recurrent obstruction. It does not increase longevity, but x-ray therapy will usually relieve temporarily the pain from metastasis or perineural infiltration.

11. Radical perineal prostatectomy actually offers a prospect of cure but has thus far been rendered ineffective by its low rate of applicability.

#### REFERENCES

- BARRINGER, B. S. Prostatic carcinoma. *J. Urol.*, 33: 616-620, 1935.  
 BUGBEE, H. G. Unsuspected carcinoma of the prostate discovered on section. *J. Urol.*, 22: 363, 1929.  
 BUGBEE, H. G. Experiences with transurethral resection in carcinoma of the prostate. *Tr. A. A. G. U. Surgeons*, 29: 207-212, 1936.  
 BUMPUS, H. C. Clinical study of 1000 cases of carcinoma of the prostate. *Surg., Gynec. & Obst.*, 43: 150-155, 1926.  
 CAULK, J. R. Carcinoma of the prostate. *J. Urol.*, 37: 832-839, 1937.

- CAULK, J. R. Transurethral surgery. *Surg., Gynec. & Obst.*, 58: 341, 1934.  
 CHWALLA, R. Beitrag zur Therapie des Prostatacarcinoms. *Ztschr. f. urol. Chir.*, 38: 154-160, 1933.  
 COLSTON, J. A. C., and LEWIS, L. G. Carcinoma of the prostate, a clinical and pathological study. *South. M. J.*, 25: 696-700, 1932.  
 CUNNINGHAM, J. H. Treatment of carcinoma of the prostate. *Boston M. & S. J.*, 186: 99-105, 1922.  
 DOLAN, L. P. Carcinoma of the prostate. *Urol. Corresp. Club Letter*, June 6, 1938.  
 DUBLIN, L. J., and LOTKA, A. J. Length of Life. New York, 1936. Roland Press.  
 DUFF, J. Cancer mortality, bladder, kidney, and prostate, 1917-1928. *J. Urol.*, 32: 346-353, 1934.  
 FERGUSON, R. S. Recent advances in diagnosis of carcinoma of the prostate. *Canad. M. A. J.*, 29: 497, 1933.  
 GRAVES, R. C., WARREN, S., and HARRIS, P. N. Osseous metastases of carcinoma of the prostate with special reference to the perineural lymphatics. *Tr. A. A. G. U. Surgeons*, 29: 179-205, 1936.  
 HIRSCH, E. F., and SCHMIDT, L. E. Small carcinoma of the prostate gland. *J. Urol.*, 20: 387-405, 1928.  
 JACOBS, A. Transurethral resection of the malignant prostate (with a review of 15 cases). *Brit. J. Urol.*, 7: 321-329, 1935.  
 KEYES, E. L., and FERGUSON, R. S. Early diagnosis and radical treatment of carcinoma of the prostate. *Brit. J. Urol.*, 8: 346-352, 1936.  
 MARION, G. Treatment of cancer of the prostate. *J. d'urolog. méd. et chir.*, 21: 385-396, 1926.  
 Metropolitan Life Insurance Company. *Statistical Bulletin*, 19: 2-4, 1938.  
 MOORE, R. A. Morphology of small prostatic carcinoma. *J. Urol.*, 33: 224, 1935.  
 MUIR, E. G. Carcinoma of the prostate (Hunterian Lecture). *Lancet*, 1: 667, 1934.  
 RICH, A. R. On frequency of occurrence of occult carcinoma of the prostate. *J. Urol.*, 33: 215, 1935.  
 STIRLING, W. C. Treatment of prostatic cancer. *South. M. J.*, 27: 590-597, 1934.  
 SWAN, C. S., and MINTZ, E. R. A review of the prostatectomies for benign hypertrophy at the Massachusetts General Hospital. *J. Urol.*, 26: 67-90, 1931.  
 THOMPSON, G. J. Transurethral resection. *J. Urol.*, 3: 405, 1935.  
 THOMPSON, G. J., and EMMETT, J. L. Treatment of carcinoma of the prostate by transurethral resection. *Urol. & Cutan. Rev.*, 39: 679-685, 1935.  
 VON ILLYES, G. Erfahrungsergebnisse bei Nieren-, Blasen-, and Prostatakrebs. *Ztschr. f. urol. Chir.*, 41: 123-132, 1935.  
 YOUNG, H. H. The radical cure of cancer of the prostate. *Surg., Gynec. & Obst.*, 64: 472-484, 1937.



# SPONDYLARTHROSIS DUE TO POSTURE AND ITS TREATMENT

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THE belief is widespread that, due to the position of the human body, the vertebrae as the carriers of weight are readily subjected to arthritic changes. Since we know, however, that the vertebrae of chickens occasionally also show osteoarthritic involvement, we can disregard all theories that attribute spondylarthrosis to the erect posture of human beings. According to some authorities the frequency of spondylarthrosis is due to repeated shocks sustained through modern transportation.

The condition is generally regarded as a form of rheumatoid arthritis, mostly of infectious origin, associated with fibrositis of the muscles of the back. These assumptions are responsible for various therapeutic procedures for so-called back pain, lumbago, etc.

A careful check-up showed that spondylarthrosis is not a disease of the working class, but apparently runs in certain families. We have x-rayed a great number of children whose parents suffered from this condition, and found that the majority showed an hereditary malformation of the epiphyseal ring of the vertebrae. As a result of these changes, uneven ossification of the epiphyseal ring occurs, causing unequal distribution of weight upon the vertebrae and, ultimately, the condition known as kyphosis or scoliosis of the vertebral column.

In view of these facts, corroborated by Scheurman and Kienbock, it is erroneous to assume that kyphosis of juveniles is caused by incorrect posture at school. It is organic insufficiency which causes a discrepancy between the load and carrying capacity of the vertebrae and which finally results in what we call juvenile kyphosis and scoliosis.

It is known that between the vertebral bodies there are discs composed of elastic

fibers and that such intervertebral discs are instrumental in transmitting and balancing the pressure of weight from one vertebral body to the other. The fact has been established that these discs, due to deformity resulting from a fracture of the vertebrae for instance, resume their original form upon elimination of pressure.

It may be of interest to note that the intervertebral discs of the cervical spine have a capacity of sustaining 155 pounds of weight; those of the dorsal, 215; and those of the lumbar, 410 pounds. It has further been established that the height of an average person is 16 mm. less in the evening as compared with the morning—this fact being determined by compression of the intervertebral discs.

It is evident, therefore, that as long as the intervertebral discs preserve their elastic properties, no definite changes in the bony structure will occur on the side of greater pressure, as occurs in kyphosis and scoliosis. However, as soon as the elasticity is diminished, induration of the disc edges set in, with a tendency toward proliferation in the defective areas of the vertebral bone. Such changes, in conjunction with abnormal distribution of weight due to posture, cause a widening of the joint capsules, and hence a loosening of the intervertebral articulations. The process of repair soon begins in such loosely connected joints, and a small bony proliferation is first observed at the contiguous edges of the vertebrae. The proliferation of bone as observed in osteoarthrosis is consequently nothing but a process of reparation, with the ultimate tightening of intra-articular connections through bony bridges. The early recognition of initial changes therefore is of utmost importance; and the detection of minor nodules revealed by x-ray examination should be carefully

considered even in the absence of subjective complaints.

In view of the foregoing facts, we definitely disregard the concept of toxic infectious origin of spondylarthritis, except in cases of polyarthritis and those of tuberculous or typhoid origin.

As the process of progressive destruction is generally unaccompanied by either pain or discomfort, even in the late stages in the presence of x-ray evidence of bony bridges, the patient remains skeptical as far as his relation to the disease is concerned.

Early diagnosis is of utmost importance, and we therefore believe that all cases of scoliosis in young persons should be subjected to x-ray examination. In the majority of these cases no definite changes of bone will be noted. It should be borne in mind that proliferation of the edge of the intervertebral disc and the change in the width of the intervertebral spaces are the first signs of the onset of spondylarthritis. Over a long period we have made 1,652 x-ray examinations of spines in adolescents in which we were suspicious of such changes. Over 865 of this number were advised to report every year; the others did not show any appreciable x-ray findings. However, due to the fact that x-ray pictures could only be taken in two dimensions (anteroposterior and lateral), there still remains the possibility that some change might have been present. Only stereoscopic x-ray pictures could definitely exclude such possibilities.

#### TREATMENT

During the early stages of this affection, attention is chiefly directed toward the correction of posture through exercise, mainly creeping, and the strengthening of the soft connective tissue of the vertebrae. Realizing that arthritic changes in the form of ultimate bridging is but a process of repair based upon modification of loosened articulations, we have successfully employed injections of autogenous blood, administered in the joint capsules in a fan-like fashion, the organization of the blood content resulting in the tightening

of the capsules. Local hyperemia and vitamin administration are likewise essential.

**CASE I.** A girl 12 years of age complained of a tired feeling in her back, associated with a sensation of cold. Objective findings were slight scoliosis of the upper dorsal vertebrae with marked tenderness upon pressure and atrophy of the muscles of the back. X-ray examination showed scoliosis of the second to the eighth dorsal vertebrae, with convexity to the right, but no evidence of bony changes. The intervertebral spaces between the third, fourth, fifth and sixth dorsal vertebrae were definitely diminished. Stimulation of the muscles and active exercise were advised. The patient was under observation for five years, and had no complaint during this time.

**CASE II.** A young woman, 18 years of age, with amenorrhea, was subject to frequent colds, usually culminating in very definite pain around the chest and back. No muscle atrophy was present, but there was very definite scoliosis of the dorsal vertebrae, with limitation of motility of the entire dorsal spine. X-ray examination showed the fifth, sixth, seventh, eighth and ninth dorsal vertebrae markedly changed in bony structure, with slight lipping. Corrective exercises and routine treatment alleviated the pain and discomfort. In all probability, however, bony bridging will take place within a few years, the changes having been too far advanced for preventive measures.

**CASE III.** Male patient seventeen years of age complained of being easily worn out and tired. Muscles of the back showed definite atrophy and slight scoliosis of dorsal spine. X-ray examination showed kyphoscoliosis of the dorsal vertebrae. There was a definite narrowing of the intervertebral spaces of the entire dorsal and lumbar area. In this case the intervertebral disks had lost their elasticity. Three years later, after corrective exercises and support, x-ray examination revealed definite improvement.

The following three cases typify the late stages of spondylarthritis:

**CASE IV.** A male patient, 63 years of age, a porter, generally carried loads of 200 to 250 pounds on his shoulder, with no complaint of pain. This patient slipped and fell on his buttocks. The fall was followed by pain in the left sciatic nerve. The lumbar spine was stiff and painful on pressure. X-ray examination

revealed spondylarthritis and definite changes in the structure and shape of the bone. The third lumbar vertebra appeared completely compressed and bony bridging was evident throughout the lumbar vertebrae.

CASE V. A male patient of 60 years, a broker, complained of spastic pain in both legs for two years. He had no recollection of having had any accident or previous pain. Complete stiffness of the dorsal spinal and lumbar vertebrae was present. X-ray examination showed definite changes in the shape and structure of the tenth, eleventh and twelfth dorsal vertebrae, and a wedge-shaped deformity of the twelfth vertebrae. The lumbar vertebrae showed spondylarthritis with bony bridging.

CASE VI. A man 60 years of age, who was occupied in the unloading of trucks, had no previous history of any diseases. Two months previous to examination the patient started to complain of pain in the back, which developed shortly after a sore throat. There was definite immobilization of the dorsal vertebrae, and pain on pressure over this area. X-ray examination showed fusion of the vertebral bodies, the vertebral arches missing, and the vertebral canal open. A diagnosis of spina bifida occulta was made.

These and many similar cases show a wide discrepancy between objective and clinical findings. Although patients denied the occurrence of pain, it may be assumed with impunity that, within these long periods, some rheumatoid pain was present at one time or another. It may be of interest to add that precordial and abdominal pain may be caused by irritation of the roots of their respective segments, which may be traced back to arthritic changes in the vertebrae. This type of case deserves special interest, in view of the fact that various manipulations of the spinal column have cleared up symptoms which did not yield to medical treatment.

CASE VII. A male patient, 40 years of age, complained for six years of precordial pain associated with palpitation. Electrocardiographic findings of the heart were negative. The patient fell while skating and injured his back. X-ray examination of the spinal column revealed no injury, but showed bony bridging of most of upper dorsal vertebrae. The changes

between the fifth and sixth dorsal vertebrae were especially marked and showed evidence of osteoporosis and almost complete lack of the intervertebral space. Orthopedic support and local treatment have almost completely cleared up the cardiac symptoms.

CASE VIII. A man, 51 years of age, complained of pain in the abdomen, especially in the evening. X-rays of the intestines showed no changes. The patient was put on various diets, without result. Pain persisted for seven years and gradually became worse. After an automobile accident, the patient had contusions of the back. At this time he complained of severe pain radiating from the lumbar region into both legs. It is interesting to note that the abdominal pains almost entirely ceased after the automobile accident.

Examination revealed complete stiffness of the spine beginning about the sixth dorsal vertebra. X-rays showed spondylarthritis of the dorsal spine beginning at the seventh vertebra, and similar changes between the first, second, third and fourth lumbar vertebrae. There was marked lipping of the seventh, eighth, ninth and tenth dorsal vertebrae. The x-rays further revealed ptosis of the stomach, which had apparently developed secondarily. Orthopedic support and local treatment have alleviated pain. The patient was observed over a period of three years.

CASE IX. A woman, 30 years of age, complained of general weakness for years. Posture had been poor since childhood. For six months the patient had complained of paresthesia in both hands, associated with numbness of the fingers. Elevation of the arms relieved the paresthesia. Marked scoliosis of the upper dorsal spine was associated with pain on pressure over this area. X-ray examination revealed slight bony lipping of the third, fourth, sixth and seventh vertebrae and distinct scoliosis of the upper dorsal spine. Local treatment of the cervical plexus alleviated patient's complaint.

Bony proliferation causes a venous hyperemia in the intervertebral venous plexus, resulting in chronic irritation of the root of the nerves in the affected area. This condition produces a point of minor resistance and, therefore, any focal infection may bring about acute inflammation.

It has been our experience that even the gravest forms of spondylarthritis may per-

sist for decades, without any symptoms. Major symptoms invariably develop in consequence of foci or trauma, and present a difficult problem. The symptoms in such cases range from local back pain to referred pain along such nerves whose roots might be affected. Consequently various regions such as extremities, abdomen, precordium, etc., may be the site of complaint.

The method of therapeutic procedure is twofold:

1. *Mechanical.* Elimination of pressure to the highest possible degree, through the application of a belt, and orthopedic exercises as well as stimulation of atrophied muscles, to strengthen interarticular connections.

2. *Chemical.* Administration of drugs known as anti-arthritic remedies, which alleviate pain.

As pain in such cases is invariably due to inflammatory processes in the nerve root, it is natural to apply the method of nerve-blocking by injecting the affected areas with large quantities (1, per cent) of procaine solution. In some cases x-ray irradiation has been successfully employed. We have been obtaining more than satisfactory results by infiltrating such areas with animal serum as a foreign protein. For the past year and a half we have also been resorting to the administration (local infiltration) of a preparation consisting of organic sulfur, iodine, and a local anesthetic. Although this preparation has been used for a relatively short period of time, it appears to be of value, and may be administered as an adequate substitute for procaine.

We are of the opinion that major symptoms of spondylarthritis are most satisfactorily treated by the infiltration method. Cases of simple spondylarthritis, on the other hand, are amenable to bee venom therapy. Local hyperemia in the form of baking, diathermy, and short wave have been found useful adjuvants.

#### SUMMARY

It has been shown that hereditary malformation of the epiphyseal ring of the

vertebrae is the determining factor in pathologic juvenile posture. The most frequent form of spondylarthritis develops as a reaction to such postural changes.

The function of the intervertebral disc is described. It is pointed out that as soon as the elastic properties of these discs are diminished, a narrowing of the intervertebral spaces sets in, as the first step toward the development of spondylarthritis. As shown in the case histories, no complaints are usually present at such an early stage. It is, nevertheless, important to administer treatment, in order to prevent loosening of the soft connective tissues. As soon as the capsules of such articulations become loosened, the vertebral column loses its firmness and a proliferation of bone on the edge of the vertebrae occurs, with the tendency to form bony bridges and to produce tight interarticular connections.

Arthritis, and especially spondylarthritis, if not of infectious origin, is therefore regarded as a form of reparation, with a tendency to tighten interarticular connections wherever the joint capsules become loosened.

Therapeutic measures based on such etiology of spondylarthritis are described.

#### REFERENCES

- AMEROMI, R. G. Pathology of adolescent scoliosis. *Brit. M. J.*, 1: 215, 1938.
- DE MAILLÉ, G. Apropos des infiltrations de novocaïne. *Soc. de med. mil. franc.*, 31: 482, 1937.
- DE MOST, M. A. Procaine infiltration (méthode Leriche). *Bull. med. de Paris*, 51: 323, 1937.
- KLAIP, R. The functional treatment of scoliosis. Jena, 1910. Fischer.
- KLEINÖCK, R. X-ray diagnosis of bone and joint diseases. Urban and Schwarzenberg, 1933-1938.
- KRETSCHMARG, S. Backache. *M. Rec.*, 149: 5, 1939.
- LABAT, L. G. Regional anesthesia. In *Cyclopedia of Medicine*, vol. 1: 496, 1931.
- KOPSTIN, G. Finding on processus spinosus by back pain. *Fortschr. u. d. Geb. d. Roentgenstr.*, 56: 14, 1937.
- LERICHE, R. *Traité de chirurgie orthopédique*. Paris, 1937.
- LERICHE, R. *The surgery of pain*. London, 1939. Baillière.
- VIDAL-NAQUET. Procaine infiltration of symp. ganglion in rheum. *Hospital*, 1937.
- OPPENHEIMER, A. Diseases of epiphyseal articulations. *J. Bone & Joint Surg.*, 20: 285, 1938.
- WILLES, P. Postural deformities of antero-posterior curve. *Lancet*, 1: 911, 1937.

# CASE REPORTS

## CONGENITAL ARTERIOVENOUS ANEURYSM OF RIGHT UPPER EXTREMITY\*

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**A**RTERIOVENOUS aneurysm is not a surgical curiosity, having been first accurately described by William Hunter in 1757 (Reid<sup>1</sup>). These cases of congenital arteriovenous anastomoses are so very rare that it is important to report all such cases.

### CASE REPORT

The patient, a 28 year old Negro man, was admitted to the Surgical Service of Harlem Hospital on November 6, 1935, complaining of a progressive enlargement of the right hand and arm, which he had noticed for fifteen years. At the age of four he had received a laceration of the volar surface of the right wrist, for which no medical attention was required. Nine years later he first noted a slight enlargement of the right upper extremity, which he thinks began shortly after he cut his right little finger. Since that time the extremity had steadily increased in size, so that the right arm was about twice as large as the left when dependent, but shrank to nearly normal size when raised above the head. The veins of the right hand and arm had grown very large and tortuous. The arm was much warmer than the left and the right hand perspired profusely. Two years before admission the patient suffered a laceration of the distal phalanx of the right fourth finger, since which time this finger had been painful and tender to pressure, and the soft parts of the distal phalanx had atrophied. Since this injury the patient had been unable to make a tight fist with his right hand. During the year before hospitalization he complained of an aching pain in the midportion of the right arm, most noticeable while lying down. The patient's general health had been excellent;

he had never suffered any severe constitutional disease, nor had he complained of dyspnea, orthopnea, persistent cough, chest pain or edema of the lower extremities.

Physical examination disclosed a well developed young man appearing in good health. In the suprasternal notch arterial pulsations were visible. The lungs were normal. The heart was not enlarged to percussion; the maximum apex impulse was in the fifth left intercostal space 1 cm. within the midclavicular line. Heart sounds were of good quality, forceful, with regular sinus rhythm, rate 84; no murmurs were audible. The abdomen and reflexes were normal.

There were no abnormalities of the extremities except the right arm. This was longer than the left by 4 cm. The circumference of the forearm was greater than that of the upper. The entire hand, forearm and medial portion of the arm showed a large number of tremendously dilated, tortuous, easily compressible veins, which filled to tenseness when the arm was lowered and almost completely emptied when the arm was raised above the head. There were three small hemispherical subcutaneous, easily compressible masses on the dorsum of the arm and the right chest wall. (Figs. 1 and 2.) There was a 3 cm. hairline scar on the volar surface of the right forearm 2 cm. above the wrist joint. The skin on the palmar surface of the hand was wrinkled longitudinally. There was atrophy of the soft tissues of the distal phalanges of the 4th and 5th fingers. There was a pronounced thrill over the dilated vessels on the volar surface of the forearm, most marked on the radial side 5 cm. above the wrist. A loud to-and-fro murmur was audible at this point, and a single murmur in the upper part of the forearm. Both the thrill

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and the murmurs disappeared with slight pressure at the point of maximal thrill.

Blood pressure in the right arm was 140/90,

of the hand there were many "vacuoles," interpreted by the roentgenologist as due to "pressure from varices." X-rays of the hand

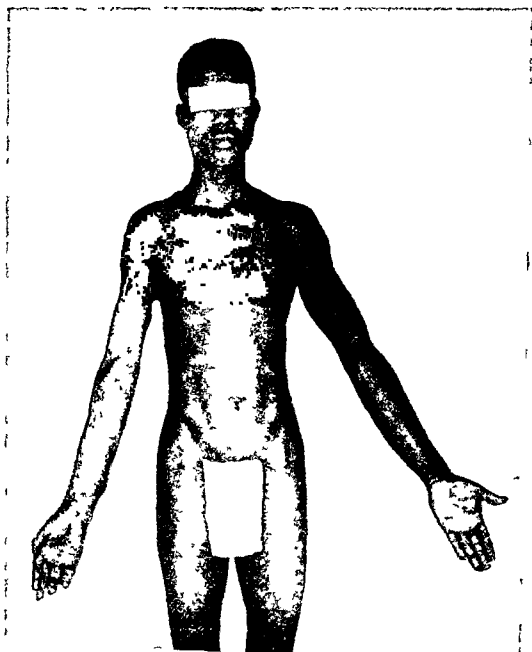


FIG. 1. Note large number of engorged, tortuous superficial vessels in right forearm and arm and increase in length of right arm.



FIG. 2. Note emptying of large superficial blood vessels of right forearm when arm is elevated.

in the left 140/100. Oscillometric readings were as follows:

	Wrist	Upper Forearm	Arm
Right	20 plus	20 plus	20 plus
Left	10	25	3.0

Laboratory examinations showed the following data: Hemoglobin 90 per cent; R.B.C. 4,500,000; W.B.C. 7,200; polynuclears 72 per cent; lymphocytes 25 per cent; mononuclears 3 per cent; urine examination was normal; blood Kahn was strongly positive. X-ray of the chest showed slight enlargement of the heart to the left. Electrocardiogram revealed no evidence of myocardial damage. X-rays of the arms and hands showed the left to be normal. The bones of the right arm and hand were larger than normal; they showed abnormally large foramina for the nutrient vessels; there was rarefaction of the bones of the hand and arm, with irregular atrophy of all the small bones about the joints. The right fifth metacarpal was smaller than the first. In the bones

and forearm following injection of the superficial veins of the hand and of the brachial artery just below the elbow with various radiopaque media showed a large number of greatly dilated and tortuous vessels. No definite arteriovenous communication could be demonstrated. Venous pressure in the right midforearm was 280 mm. of water, in the left antecubital fossa 150 mm. Carbon dioxide combining power of blood obtained from the right brachial artery was 37.26 volumes per cent, and of blood from the left cephalic vein 65.02 volumes per cent.

The patient was operated on December 27, 1935, the preoperative diagnosis being arteriovenous aneurysm of the right radial artery. The brachial artery was exposed at the elbow and temporarily ligated with rubber bands. A 10 cm. linear incision over the radial artery just above the wrist exposed many large superficial vessels, which were dissected and ligated. There were numerous adhesions between the tendon sheaths of the flexors and the subcutaneous tissue. A large, thin-walled, pulsating vessel was found at the site of the radial artery; this vessel was followed upwards for 10 cm., becoming larger and more tortuous



proximally, but no abnormal anastomoses were found. It was ligated and a portion excised for section. Incision over the lower part of the

had not increased since operation. He felt an annoying buzzing sensation throughout the forearm. He complained of dyspnea after



FIG. 3. X-ray of hands, showing overgrowth of bones of right hand, mottling and atrophy of distal phalanges.

ulnar artery revealed similar thin-walled, dilated and tortuous vessels. Microscopic section of the excised vessel showed the structure of a normal artery, but all layers of the wall were thinned. The postoperative course of the patient was entirely uneventful. Healing was by primary intention. Two days after operation no bruit was audible nor thrill palpable. The arm when dependent was much smaller than before operation; the swelling of the vessels was about half as much as formerly. The patient stated that the arm did not feel so heavy as before the operation. He was discharged two weeks after operation markedly improved.

The patient was readmitted to the hospital on November 15, 1936. At this time he stated that he had done well until four weeks before, all of his symptoms being much improved by the operation. In the previous month, however, he had suffered increasingly severe pain in the tip of the right fourth finger, associated with steadily increasing swelling of the finger. Two weeks prior to admission the nail of the finger had sloughed off. The pain had been so agonizing for two weeks that the patient asked to have the finger amputated if the pain could not be quickly controlled. The size of the arm

moderate exertion, not severe, but steadily progressive in the preceding six months.

Physical examination revealed the following salient points: The heart was enlarged to 1 cm. outside the midclavicular line, the apex impulse being felt in the 6th intercostal space; there was a soft systolic murmur at the apex. The pulse was 90, the blood pressure in both arms 130/90. The right hand was one and a half times as large as the left, the skin dry and wrinkled, and there was a foul ulceration involving the distal phalanx of the fourth finger. There was a well-healed scar over the right radial artery, and no pulsation, thrill or murmur was detected over its course. Over the ulnar side of the forearm, however, extending up to the elbow, there was a pronounced thrill with a loud to-and-fro murmur. There were, as on the first admission, numerous dilated and tortuous veins throughout the forearm, arm, and upper half of the right chest. Several small, soft, hemispherical, subcutaneous and freely movable non-tender masses were present in the arm and right chest wall.

Laboratory data showed: urine normal. Hemoglobin 70 per cent; R.B.C. 3,660,000; W.B.C. 7,600; polynuclears 67 per cent; lymphocytes 25 per cent; mononuclears 8 per

cent. Blood Kahn was 3 plus. Blood chemistry was: creatinine 1.1; urea nitrogen 14.7; sugar 78. X-ray of the chest showed the heart to be

the forearm, thus probably placing some abnormal arteriovenous communication in this area.



FIG. 4. Section from artery in right arm, showing degenerative changes in media.

enlarged to the left and downward, with the lungs clear. X-ray of the right hand showed "atrophy of the bones, with narrowing of the joint spaces and numerous erosions throughout, due to arteriovenous aneurysm." (Very similar to x-ray on first admission.) In an attempt to localize any abnormal arteriovenous connections in the arm, specimens of blood were taken from the veins of four segments of the extremity, following the technique described by Veal and McCord<sup>2</sup> of the Mayo Clinic. These values were obtained:

	Dorsum of Hand	Lower Half of Forearm	Upper ¼ of Forearm, Lower ¼ of Arm	Middle Half of Arm
CO <sub>2</sub> vols. per cent . . . . .	37.02	36.50	42.02	46.17
O <sub>2</sub> vols. per cent	31.38	30.42	21.41	28.63

These results appear to show the presence of blood nearly arterial in character in the veins of

Operation was performed on December 30, 1936. Having dissected the radial side of the forearm at the first sitting a year previously without finding any evidence of direct arteriovenous communications, we believed that a second operation over the ulnar vessels would be similarly disappointing both as to finding pathology and affording relief to the patient. We felt, too, that a sharp reduction in the supply of arterial blood to the limb would bring about marked subjective relief and would postpone the day when amputation of the arm (which appeared eventually inevitable) would have to be done. Under ether anesthesia the antecubital space was dissected. The subcutaneous tissues were filled with a large number of enormously dilated, tortuous and thin-walled veins, the vena mediana cubiti and the basilic vein being the largest, the former measuring 2 cm. and the latter 1.5 cm. in diameter; no arterial pulsation was noted in these veins. The brachial artery was isolated for a distance of 5 cm.; it appeared somewhat thinner-walled and more friable than normal. No direct arteriovenous communications were encountered. The brachial artery and the vena

mediana cubiti were ligated and a 5 cm. segment of each was resected. In addition, one of the spongy soft tissue masses described above was removed from the subcutaneous

amputation of the arm would be necessary as a life-saving measure. This procedure was urged on the patient, but at this time he refused such radical treatment.



FIG. 5. Roentgenogram after injection of right radial artery with 50 per cent sodium iodide, showing marked increase in vascularity of right forearm and hand.

tissue over the belly of the triceps muscle, as well as two small sections of the muscle for microscopic examination. The incisions were closed without drainage. Healing was prompt.

At no time after operation was any pulsation felt in the arm below the elbow. There was immediate and marked subjective relief, in that the patient had much less pain in the hand and arm, and no longer was troubled by the constant buzzing sensation which had previously been so annoying. On the fifth post-operative day the patient complained of severe steady pain at the tip of the fourth finger, which showed a slight spread of the soft dark slough present on admission. This pain was controlled with small doses of codeine for several days, but two weeks after operation was so intense that he asked to have the finger amputated. At this time there was a further slow spread of gangrene down the fourth finger, as well as small gangrenous spots on the tips of the second and fifth fingers. Amputation of the fingers or hand was not done because it was felt that in the presence of the impaired circulatory status of the limb healing would not take place. On discharge of the patient one month after operation, there had been no further spread of gangrene, and the pain in the hand had completely subsided, so that he felt somewhat improved by operation. We knew, however, that the pathology had not been eradicated, and believed that eventually high

Microscopic examination of the specimens removed at the second operation showed (1) a normal brachial artery; (2) an increase in the smooth muscle fibers in the walls of the vena mediana cubiti; (3) normal striated muscle; and (4) the soft tissue mass, designated an arteriovenous angioma. The sections showed tissue composed almost entirely of blood vessels most of whose walls were only one cell thick; a few small vessels with the structure of small arteries and veins were seen. No cells were seen which appeared definitely neoplastic in character.

Following the last discharge from Harlem Hospital, this man suffered increasingly severe pain in the right hand and forearm, and there was a slow spread of gangrene up the hand. In February of 1937 the arm was amputated in an Elizabeth, New Jersey hospital, the amputation being done at the mid-shaft of the humerus. (Unfortunately no pathologic study of the amputated extremity was made.) Relief of all symptoms followed immediately and has continued to the present time. He states that he feels better than at any time in the past four years. All cardiac symptoms have completely disappeared. The amputated stump is completely healed and the patient wears an artificial limb. There are still a few slightly dilated superficial veins in the arm and shoulder, but there is no abnormal arterial pulsation, and no other apparent difference between the

upper halves of the arms. Whether or not the process has been permanently arrested I cannot say at this time; certainly the man is clinically well, eighteen months after amputation.

#### COMMENT

This case is interesting from several standpoints, first as to diagnosis. The mass removed from the arm showed angiomatic tissue, making it appear likely that the whole pathology was hemangioma of a cavernous type. On the other hand this patient's whole extremity was larger than the left arm; there was increased bone length and size in the forearm and hand. In addition, specimens of blood drawn from veins of the arm more closely approximated normal arterial than normal venous blood in their gas-carrying capacity; this fact would suggest multiple abnormal arteriovenous communications; no such communications, however, were found at either operation. Moreover, the abnormal arterial pulsations and bruits suggest the likelihood of arterial origin of the process. Mont Reid<sup>3</sup> makes this statement: "It seems certain that the impaired circulation in a case of subcutaneous cavernous hemangioma is due to the venous angioma and that, as a result of poor nourishment, the limb fails to develop normally. In this case the capillary bed is probably normal but the large angioma on the venous side of it definitely embarrasses circulation. This is in quite striking contrast to the over-development that may result from cirroid aneurysms; in cirroid aneurysms there is an overabundance of arterial blood without any obstruction to venous return."

Hemangiomata of various parts of the body are not rare, being repeatedly described as occurring in the skull, the liver and skeletal muscle. Jenkins and Delaney<sup>4</sup> collected a series of 254 cases of hemangiomata of skeletal muscle. All of these, however, were directly traceable to a definite origin in some particular vein or small group of veins. Most of them were definitely encapsulated tumor masses.

This case, in contradistinction to those described by Delaney, is one presenting a diffuse process involving a whole extremity, and no origin in any one vein, or artery either for that matter, could be found. So diffuse a disorder, if indeed it be an hemangioma, is very rare. Definite proof of the type of lesion is missing because of the failure to dissect and study the amputated arm.

The senior author has performed twelve operations in which the subclavian artery and vein were anastomosed for the relief of aortic aneurysm. This is a modification of Babcock's operation, in which he made an arteriovenous fistula between the common carotid artery and the internal jugular vein. The patients that survived this procedure eventually died of heart failure due to the strain thrown on the heart by the fistula. The clinical picture, however, so completely fits the criteria for diagnosis of arteriovenous aneurysm of congenital origin, that we are justified in considering this case one of congenital arteriovenous aneurysm. Seeger,<sup>5</sup> in an exhaustive treatise on the subject of congenital arteriovenous anastomoses, describes just those findings presented above as diagnostic of congenital arteriovenous aneurysm, namely, hypertrophy of soft tissues and bones, increased oxygen content of venous blood, increased temperature of the skin of the extremity, and venous dilatation.

#### CONCLUSION

The presence of an arteriovenous fistula demands complete extirpation of the fistula or fistulae, for cure. In some instances it is possible locally to remove the lesion and save a limb. If the pathologic process is too extensive, then amputation is indicated if the patient's life is to be saved.

#### REFERENCES

1. REID, MONT. *Arch. Surg.*, 10: 601-638, 1925.
2. VEAL, J. R., and McCORD, W. M. *Arch. Surg.*, 33: 848-866, 1936.
3. REID, MONT. *Am. J. Surg.*, 14: 46, 1931.
4. JENKINS, H. P., and DELANEY, P. A. *Surg., Gynec. & Obst.*, 55: 464-480, 1932.
5. SEEGER, S. J. *Surgery*, 3: 264-305, 1938.

# DILATED MOBILE CECUM WITH VOLVULUS SIMULATING INTRA-ABDOMINAL CYST

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WHILE numerous studies and case reports of volvulus of the cecum and cecocolon have been published, the writers have seen no case report with roentgenographic and roentgenoscopic findings such as are found in the case herewith reported. Indeed, very few of the case reports are accompanied by illustrations of the Roentgen findings. Most writers concede that volvulus of the cecocolon is dependent on failure of the primitive mesentery of the cecum to become adherent to the posterior peritoneum. This leads to a mobile cecum, the degree of mobility being proportionate to the length of the mesentery. In extreme cases, the ascending mesocolon may be continuous with the mesentery of the small intestine, resulting in the condition known as mesenterium commune. The embryologic defects leading to mobile cecum have been fully discussed by many writers.<sup>1,2,3</sup>

Once present, a mobile cecum is a potential source of volvulus, dependent upon such factors as indiscretion of diet, distention of the cecocolon by gas, excessive exercise, drastic catharsis, and similar mechanical disturbances.

Volvulus occurs mainly through a vertical axis with rotation in a clockwise direction. The resulting symptomatology and pathology depend upon the degree of torsion. If the torsion is less than 180 degrees, the obstruction may be incomplete and the circulation to the cecocolon may not be interfered with excessively. If the torsion is over 180 degrees, the obstruction may be complete and gangrene may result.

Some writers divide their cases into acute and chronic, the latter being more

common and generally giving obscure symptoms of intermittent obstruction. The acute cases occur much less frequently (1.15 per cent of all cases of acute intestinal obstruction in Massachusetts General Hospital from 1873 to the present<sup>4</sup>).

The diagnosis of the acute cases is seldom made preoperatively, contributing to a high mortality due to the delayed treatment. Occasionally the diagnosis is made more difficult by complicating factors such as pregnancy.<sup>5</sup> In the chronic cases, a history of recurrent acute attacks of pain and vomiting, relieved without operation, may suggest the diagnosis. There are cases of hypermobile cecum with a range of vertical mobility of more than 1½ inches which may give definite clinical symptoms but which cannot be included in this report since they are not associated with volvulus.<sup>3</sup>

## CASE REPORT

A white male, 54 years of age, was admitted to hospital October 11, 1937, with the following complaints: (1) nausea and vomiting for three days; (2) no bowel movement for four days; (3) pain through the entire abdomen, particularly the right lower quadrant; and (4) severe bloating and inability to pass gas.

His illness had begun about one week previous but he had been able to go about his usual duties as a farmer until three days before, at which time pain, distention, and nausea became so severe that he could no longer continue. He was unable to sleep at night but got some relief by sitting on the side of the bed and trying to induce vomiting; this caused him to eructate small amounts of gas and relieved the distention, but not the pain.

He stated that he had had similar attacks for more than five years. About three years previous, during such an attack, his case was

diagnosed as acute appendicitis; the surgeon opened his abdomen but closed it at once without even removing the appendix. He did not

lower quadrant of the abdomen revealed no peristalsis.

Laboratory tests showed 4,500,00 red cells



FIG. 1. Barium enema. Note triangular shadow at site of volvulus, simulating ileum.



FIG. 2. Note triangular shadow, described in Figure 1, now leads into a distended cecum.

know what was found at the time of this operation, but within three months he had a similar attack in another city. The hospital authorities of the second city, after communicating with the original surgeon, decided to treat him with enemas and purgatives. Since then he had treated himself in a similar manner; however, this treatment had been getting less satisfactory with each attack. The last two attacks had been extremely severe and the present attack was the most severe of all. He had always been quite constipated and had had to use heavy doses of cathartics almost daily.

Physical examination showed a slender, moderately nourished white male, very critically ill. Head, neck and chest were negative except for slight coarse bronchial breathing. The abdomen was markedly distended. There seemed to be a tumor mass just to the left and slightly superior to the umbilicus which the patient claimed could be slightly reduced by manipulation, resulting in a small amount of transient relief. This entire mass was tender when palpated. There was no absolute point of maximum tenderness, but the entire right

with 95 per cent hemoglobin, and 12,700 white cells with 89 per cent neutrophils, of which 30 per cent were staff forms and 59 segmented. There were 1 per cent basophiles and 10 per cent small lymphocytes. The urine was essentially negative. Blood and cerebrospinal fluid Kahn were negative.

In Roentgen examination of the colon by enema the barium progressed without obstruction to the colocecal region. The flexures showed no abnormality. There was tenderness over the colocecal region. On gentle pressure, a small amount of barium could be forced into a triangular shaped portion of bowel which was believed to be ileum and which subsequently proved to be the colocecal junction. (Fig. 1.) There was no distention of the coils of the small intestine and it was concluded that the obstruction was probably due to an adhesive band in the colocecal region from the previous operation. The patient was requested to expel the barium and was again fluoroscoped. He then showed a marked distention of a loop of bowel which was thought to be ileum but later proved to be cecum. (Fig. 2.)

Immediate films showed findings similar to those found on fluoroscopy. (Figs. 1 and 2.) Twenty-four hour films showed a large cyst-like

As soon as the peritoneum was opened the appendix came up into the incision. It showed only slight signs of old inflammatory reaction.

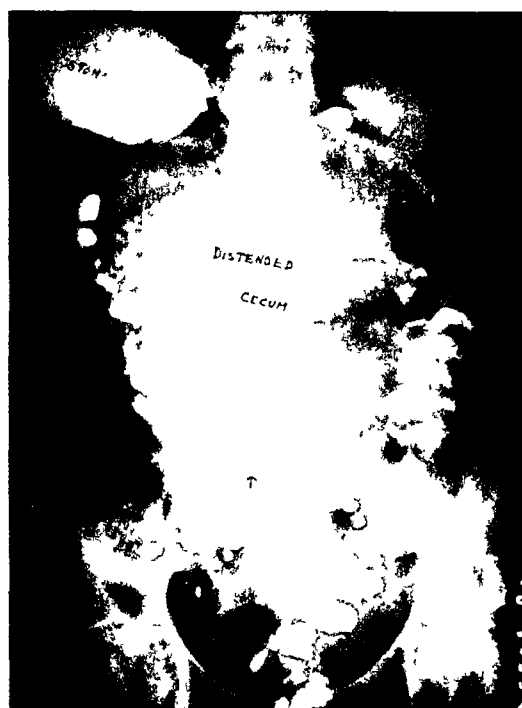


FIG. 3. Twenty-four hours after barium enema. Patient given barium by mouth. Note distended cecum simulating cyst and containing flocculi of barium.

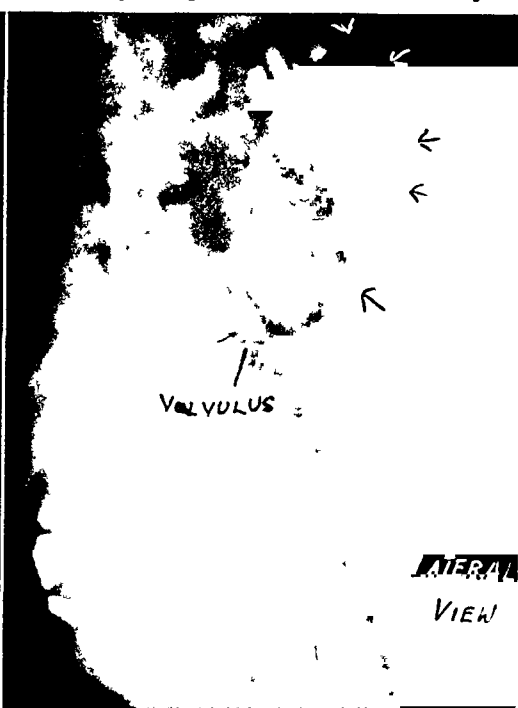


FIG. 4. Lateral view, twenty-four hours after barium enema, showing dilated cecum lying mainly anteriorly.

formation lying mainly on the right side of the abdomen and anteriorly. (Figs. 3-6.) There appeared to be a fold in the cyst-like mass and the barium was suspended as flocculi. A small amount of barium given by mouth showed no connection between the stomach and the cyst-like mass. The conclusions from the Roentgen examination were that we were dealing with either an intra-abdominal mesenteric cyst or a dilated bowel due to volvulus.

Medical treatment was not successful. Enemas did not return, and when they were syphoned off only a portion of uncolored returns could be obtained. The administration of prostigmine every two hours for six doses caused the enema to return and considerable flatus was expelled. The tumor mass seemed softer and somewhat reduced in size. However, the condition of the patient was only slightly improved and his pain was still quite marked. A preoperative diagnosis of possible mesenteric cyst was made and operation was performed three days after admission.

The abdomen was opened in the midline 2 inches above and 3 inches below the umbilicus.

The cecum to which it was attached was very markedly distended and severely rotated. Three-fourths of this tremendously distended cecum was to the left of the midline incision. Exploration revealed dense adhesions and a band formation across the colocecal junction with definite kinking of the gut. The adhesions were released and a mesentery transplant was sutured over the abraded area. The appendix, which was definitely on the anterior portion of the cecum, was removed incidentally.

Upon his awakening from the anesthetic the patient remarked about the complete relief from pain. The day following operation his condition was good. On the second day cough developed, but there was no distention of the abdomen. On the third day, postoperative lobar pneumonia developed and he died on the afternoon of the following day.

**Autopsy Findings.** The stomach, duodenum and jejunum showed no significant gross pathology. There was a dilated mobile cecum having a common mesentery with the terminal ileum. There was definite narrowing of the colocecal junction which lay about 1 inch below the iliac crest. At this point there was a

torsion of the bowel in the horizontal axis for about 135 degrees. This narrow twisted portion led into a dilated cecum which showed

the cut section was mushy. The kidneys showed some cortical cysts.

Typical lobar pneumonia was noted in

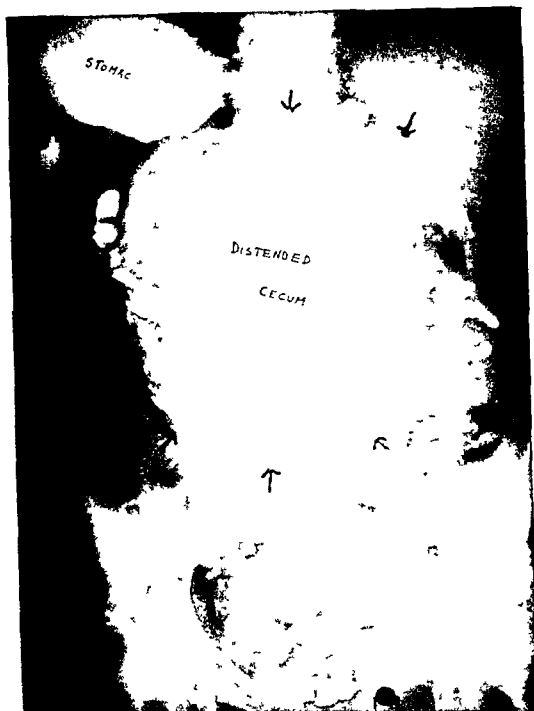


FIG. 5. Anteroposterior view, showing dilated cecum outlined by arrows.

numerous holes from the embalmer's trocar. Despite the fact that the cecum had been emptied, it still measured about 7 inches from above downward, but was flattened ventrodorsally. The appendiceal stump lay anteriorly instead of posteriorly due to the rotation of the cecum which was adherent posteriorly to several coils of ileum by a common mesentery. The colocecal junction at the point of torsion showed a thickening of the wall with hemorrhage into the wall. The mucosa was hemorrhagic. The wall of the dilated cecum itself was thin, but the mucosa grossly appeared quite normal. There were some fresh adhesions in the region of the torsion and around the appendiceal stump. The ileocolic valve appeared normal and opened posteriorly. There was no evidence of gangrene of the bowel.

Extensive massive consolidation of both lungs with the exception of the upper lobe of the left lung was noted. There was a thin fibrinous exudate over the leaves of the pleurae.

The liver was enlarged. The heart showed slight atherosclerosis of both coronaries and some dilatation of the right auricle. The spleen was enlarged to about twice normal size and



FIG. 6. Six hours after oral barium, showing gastric retention and partial filling of ascending colon. Distended cecum still visible.

microscopic study of the lungs. The alveoli were filled with red blood cells and polymorphonuclear cells. Occasional alveoli showed rupture of the walls.

Sections made of the dilated portion of the cecum showed only some fragmentation of the muscularis. Sections from the site of torsion showed edema of the submucosa, hemorrhage into the entire wall, some leucocytic infiltration of the wall and a few small abscesses in the submucosa.

#### SUMMARY

A case of mobile cecum with volvulus which roentgenographically simulated an intra-abdominal cyst, is presented. The history and physical findings suggested acute appendicitis so strongly that the patient had previously been operated on for acute appendicitis. Our Roentgen findings suggested either a large cyst communicating with the cecum, or a dilated mobile cecum. At operation the latter



condition was found. The volvulus and the adhesions (the latter probably being of embryologic origin) were released and free passage through the bowel obtained.

#### REFERENCES

- 1 PRATT, J. P., and FALLIS, L. S. Volvulus of cecum and ascending colon; report of 3 cases. *J. A. M. A.*, 89: 1225-1230 (Oct. 8) 1937.
2. GREEN, T. M. Surgical significance of derangement of intestinal rotation and distribution. *Surg., Gynec. & Obst.*, 63: 734-741 (Dec.) 1931.
3. KANTOR, J. L., and SCHECHTER, S. Colon studies; variations in fixation of cecocolon; their clinical significance. *Am. J. Roentgenol.*, 31: 751-765 (June) 1934.
4. SWEET, R. H. Volvulus of cecum; acute and chronic with reports of 8 cases. *New England J. Med.*, 213: 287-293 (Aug. 15) 1935.
5. BASDEN, M. M. Volvulus of caecum complicating labour. *Brit. M. J.*, 1: 1119 (June 23) 1934.



ALL patients with crushing injuries or contused lacerations which may be liable to develop gas gangrene should be given a routine injection of both perfringens and tetanus antitoxin.

## REGIONAL ILEITIS\*

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**A** MOST interesting case of regional ileitis came under our observation March 17, 1938. The patient was a poorly nourished, anemic young man, aged 17, 5 feet 8 inches tall, but weighing only 80 pounds. Throughout his life he had been frail, below par, undernourished, and listless. He had always been constipated but never subject to diarrhea. There was no evidence of recent loss of weight. For some weeks past his constipation had become more pronounced and he had noticed what he called "growling" in his abdomen with occasional cramping pains. In the past week the borborygmus had increased.

At our first observation this symptom could not be elicited and but little pain was present on palpation. There was scarcely any resistance or rigidity over the abdomen. There seemed to be no urgent indication for operative intervention. His physician had found on several occasions marked borborygmus and distended coils usual in intestinal block.

When the youth was next seen two days later, this latter finding was quite marked and a diagnosis of intestinal obstruction was made. The location of the obstruction seemed to be in the ileocecal region. Roentgen-ray findings were not illuminating.

At operation on March 20, 1938 the obstruction was found to be produced by a localized thickening of the terminal portion of ileum, the cecum not being involved. This portion of the ileum was bound down to the posterior peritoneum and its walls were thickened throughout all layers, constricting and closing the lumen. The lesion was at first thought tuberculous, since the resemblance to this affection was marked. On closer observation the conclusion that it was a case of regional ileitis was reached.

The patient's condition seemed to preclude an immediate resection unless a lateral anastomosis could be quickly effected. An ileocolostomy between the transverse colon and the ileum was completed. However, on an

attempt to free the mass for removal, the anesthetist advised conclusion of the effort and this advice was followed. The patient improved, his convalescence was prompt and in four months he had gained 50 pounds, to 130, was alert, with a rosy complexion and seemed well on the way to recovery.

On July 29, after complaining of some fever, sharp right-sided pain, nausea and vomiting, and physical signs of obstruction, he presented himself for operative relief. Marked tension upon the ileocolostomy was found, sufficient to cause obstruction. The anastomosis was released and after the stomata were closed in the intestinal loops, a temporary ileostomy was made.

Four days later, August 2, 1938, the terminal ileum, the cecum and the proximal third of the ascending colon with the adjacent lymph glands were resected. An end-to-side ileocolostomy was completed by suturing the open colon to a large opening in the side of the ileum, a procedure which seemed advantageous. Closure of the open small bowel was easily accomplished. The ileostomy opening was freed from its attachment to the abdominal wall and its opening was closed after evacuation of its contents by suction.

The involved loop, consisting of the terminal ileum, was thicker, firmer and less mobile than normal. It was mottled, grayish-red and sausage-like and its lumen was completely occluded. The peritoneum showed more change than at the former operation and the group of glands had increased in size and number. Above the affected loop the entire small intestine was much distended and its wall attenuated. The abdominal wound was closed in layers. The affected ileum presented a smooth, somewhat edematous peritoneal surface with some exudate about the mesenteric attachment near the ileocecal valve. On section the muscularis and mucosa were replaced in considerable degree by granulomatous tissue. The latter presented a grayish-white almost homogeneous

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avascular surface very similar to a tuberculous granuloma and a number of writers have mentioned this resemblance, notably Pemberton



FIG. 1. Gross specimen. Case 1. Terminal ileitis.

and others. It was not possible with certainty to differentiate from gross observation, between tuberculous granuloma, sarcoma or chronic regional ileitis. A more thorough study led to the diagnosis of the latter affection.

We had previously observed another most interesting case of regional ileitis of the acute type.

L. W., aged 16, male, white, was hospitalized February 10, 1936, with the history of having been annoyed intermittently with nausea, but no vomiting. During the preceding eight hours he had experienced severe pain confined to the right iliac region which had been of a paroxysmal character, radiating over the right iliac crest. There had not been an evacuation of bowel content for twenty-four hours.

A year before a similar sequence of symptoms occurred, and appendectomy had been done.

The temperature was 101; pulse 110; blood pressure 98/64 diastolic. The abdomen was quite distended, and on auscultation increased peristalsis and borborygmus were detected, rigidity was localized to the right iliac region with hyperesthesia. There was no absence of liver dulness.

Leucocytes numbered 24,000, with 90 per cent polymorphonuclears; 5 per cent lymphocytes and 1 per cent mononuclears. The specific gravity of the urine was 1.022; acid reaction and 1 plus albumin were noted.

A diagnosis of Meckel's diverticulitis with obstruction was made and immediate operation was advised.

Cyclopropane anesthesia afforded excellent relaxation and a right low rectus incision was followed by a free flow of dirty tinged fluid

accompanied by fibrin flakes. On endeavoring to deliver the ileum for inspection, in search of a Meckel's diverticulum, it was found that the terminal ileum was indurated in its complete circumference and fixed to the posterior peritoneal wall extending from the ileocecal valve for about 2 inches, with a resultant distention above. An attempt to free the terminal ileum resulted in a gush of intestinal content from a perforation which had evidently been sealed by nature's efforts. An intestinal clamp was placed on the proximal portion of the terminal ileum coincident with delivery. The parietal peritoneum lateral to the cecum was incised, the terminal mesentery of ileum was ligated and divided and 8 inches of terminal ileum and cecum was resected. A modified Mikulicz procedure was used, exteriorizing the free ends of colon and ileum with clamps through a small wound lateral to the incision. Two Penrose drains were introduced and the original incision was closed in the usual manner.

Intestinal decompression was produced by use of a duodenal tube and continuous suction.

Five days postoperatively both clamps were removed from the intestinal stumps with but slight retraction of stomata. A profuse drainage of intestinal content ensued, which was so troublesome to the patient and nursing staff that we decided on the eighth postoperative day to cut the intestinal spur. An angiotribe was introduced into both intestinal limbs and retained for twenty-four hours, after which there was a notable diminution in the fecal drainage. On the twenty-fifth postoperative day the discharge had ceased, and the patient was dismissed as recovered thirty days following operation.

*Pathologic Report.* There was a thickening of all coats of ileum from the ileocecal valve for about 2 inches, resulting in partial occlusion. The lesion was similar in consistency to a scirrhus carcinoma of the left colon, but more extensive, chronic, granulomatous inflammatory changes (hyperplastic) were noted, with fibrous tissue replacement. No evidence of tuberculosis was present. The diagnosis was chronic benign ileitis.

The literature upon this subject is quite plentiful and comprehensive, but there is as yet no agreement upon the etiology, the pathogenesis, the pathology, or even the clinical description of this form of ileitis.

Most writers hold the view that the cause of regional and also of terminal ileitis is probably bacterial even in the absence of a

"wind and costiveness" were reported. The pain was intense, the stools were small and in indurated lumps. The patient was



FIG. 2. Low power photomicrograph in Case 1.

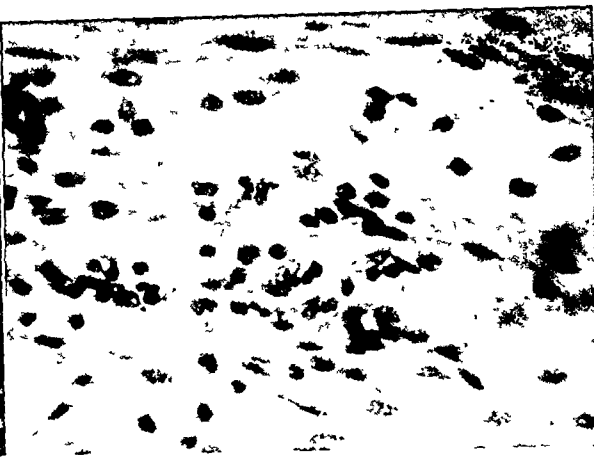


FIG. 3. High power photomicrograph.

specific organism. So far no organism has been isolated in a sufficiently large number of cases to be even suspected as the cause. The presence of *Streptococcus viridans* has been observed by some, but its causative action is not established. Intensive studies have failed to show evidence of tuberculosis as a cause. The same is true of the anaerobic streptococcus studied by Mixer, also of the bacillary causes of dysentery. It has been demonstrated that regional ileitis is not the result of Hodgkin's disease, lymphosarcoma, or other neoplasms. Neither lues nor mycotic fungi have been proved causative. That appendicitis has any direct causal relation does not seem probable, although in some instances appendicitis has preceded this affection. The presence of an appendectomy scar is placed by some among the diagnostic points. The term "intestinal granuloma" has appeared in the literature for many years and has been applied to certain lesions characterized by chronic inflammatory changes arising from different causes.

Charles Combe and William Saunders reported in full detail to the Royal College of Physicians in London, July 4, 1806, the history of the first case of this ailment. Stricture, loss of flesh, abdominal distress,

markedly emaciated in the last stages. Three distinct constrictions existed and his death evidently occurred from starvation (or inanition). The condition was considered as a benign granuloma.

It was not until 1828 that Abercrombie made his report. Nothing appeared between these dates. B. G. A. Moynihan's report was made in 1907, Braun's in 1909, and Tietze's in 1910. These writers were able to recognize the lesions as "benign intestinal granuloma" and to differentiate them from carcinomata. Crohn and his colleagues in 1932 first recorded a series of fourteen cases involving the terminal portion of the ileum and gave the name of terminal ileitis to the lesion. In many cases reported the pathologic changes are identical in the cecum with those in the ileum. The same is true of the jejunum. Three cases in that portion of the gut alone, two in the upper ileum and twenty-four in the terminal segment appear in Pemberton and Brown's series of thirty-nine cases. In eight cases more than one loop was involved (included in Sproull's report of 132 cases). Isolated areas of enteritis occur, with healthy mucosa sometimes lying in between ("skip areas") (Barber and Stokes). The concept of Crohn and his confrere that this disease affected only the terminal ileum must in the light of recent

knowledge be revised, since other portions of the intestine, both small and large, have been involved. It therefore seems best to adapt the term "regional ileitis."

#### PATHOLOGY

The pathology of regional ileitis is better understood than its causation. This is true more particularly of the chronic sclerosing cases as these come to operation and are more often seen by the pathologist. In the earlier and more acute lesions resection is less frequently done. "At this time, the affected portion of the bowel is soggy and edematous and appears hyperemic and blotchy. According to Erb and Farmer the edema may occasionally be so marked as to make the terminal ileum seem a very rigid tube. If the edema is not so severe, the bowel may feel like sponge rubber. Even in the earliest cases, the ulcerative and inflammatory changes may be definite. . . . In the later stages the acuteness subsides somewhat and a more characteristic picture is seen. The oldest portion of the lesion is usually closest to the ileocecal valve. The process extends a variable distance up the bowel and may merge gradually with normal tissue or the transition may be a sudden one. The unopened intestine appears stiff and thick and hose-like, and roughened or granular. . . . As a result of hyperplastic and exudative changes in the submucosal and muscular layers the intestinal wall may be two or three times its normal thickness. On being cut, it appears stiff and white. In the later stages exudation and edema may subside somewhat and fibrotic infiltration become marked. The thickening and contraction of the bowel wall encroaches upon the lumen and results in a gradually increasing stenosis" (Tumen).

The appendix if involved may show the same changes as the segment of the ileum. When the process extends to the colon from the ileum the pathologic process is the same. In our cases the appendix was not involved.

The microscopic picture shows no changes which may be considered as specific. For the most part these are inflammatory, but occasionally the tissue is smooth granular and may resemble a neoplasm or at least a granuloma. Occasionally giant cells are present. The lymphatic glands of the mesentery are congested, swollen and firm, but show nothing specific. The pathologic process is usually progressive but varies much in different cases. In some instances retrogression may occur, with periods of quiescence or even recovery. Ulceration and fistula formation may be seen. It is not possible in many cases to differentiate between intestinal tuberculosis, sarcoma and chronic segmental ileitis by gross study, nor is it always easy on microscopic observation to make a clean-cut differentiation.

#### ETIOLOGY

Just as the exact pathology is not identical in each case, the causative factor is unknown. It is a most interesting problem to determine why the localizing process tends to infiltration of the intestinal wall and stenosis of its lumen in some cases, while ulceration and fistula formation occur in others, with no definite difference in bacterial flora or other discernible factor. Are there different causative factors in different cases? The thought arises in the inquiring mind whether this affection with its unusual type of development, its enlarged lymphatic glands, ulceration and fistula formation in one, no ulceration in another case, may not be the forerunner of some of the obscure lymphatic and blood diseases of later life. Many anemias are far from solution. Perhaps sarcoma, known to affect the small gut most often, may find its cause and its origin in lesions of this type which have not been recognized with any frequency until very recent years. The tissue in our case was very like lymphoid tissue. Or was it not?

Since 1932 (Tumen), 200 cases have been recorded and the opportunity for study, clinical, pathologic, and etiologic, has been

great. The symptoms of the different pictures have been well described in the literature. The chief symptoms are lassitude, anemia, poor appetite, failure to gain weight, abdominal pains of cramping type, borborygmus and constipation even to obstruction in the chronic cases. Marked distention of the intestinal loops, spasmodic in type, is characteristic. Later a palpable mass over the affected loop is strong evidence of this disease. These symptoms do not differ much from those of malignant growths. In either case the indications for operative treatment are the same.

In acute cases, fever, sharp pains, diarrhea, loss of flesh and strength, with fistula formation or matting together of intestinal coils, again point to "regional ileitis" and also to malignant disease. The differentiation is not easy.

Too much cannot be said of the value of the roentgenographic study in the diagnosis of gastrointestinal lesions. Frequently, however, they show but little in these cases unless the lumen of the bowel is completely blocked. In some of the chronic cases the "string sign," mentioned by Kantor, shows the narrowed loop. Kantor advised standard opaque meals, and repeated, even hourly, examinations in the prone position from three to nine hours after the meal.

If a barium enema spills over the ileocecal valve, the deformity in the terminal loop may show. Hyperplastic tuberculosis, lymphadenoma or sarcoma of the terminal ileum will give a similar picture. Other films will show fixation of the loops and the characteristic "string sign." An abnormal picture is important even when the exact lesion cannot be definitely determined.

In ulcerative cases one would expect to find rests in addition to the findings just mentioned. Extensive fistulous changes should show considerable deformity, but often nothing is seen. Patience and repeated observation will prove worth while. The patient should not be put to needless expense, but the roentgenologist is the

best judge of what measures are necessary to obtain results. The greater his experience the better the result obtained. When a definite intra-abdominal lesion of some sort is strongly suggested by the findings, the open abdomen in competent hands offers the final solution of the problem.

Formerly, such cases seen at operation would immediately bring up the question mentioned by Pemberton and Brown, "Are you sure it is not tuberculosis?" Within recent years we have seen less of abdominal tuberculosis a compliment to curative and preventive medicine.

#### TREATMENT

The treatment of these lesions must for the most part be empiric until the cause is known. For the deformities and the stenosis so often present surgical operation is advised. Methods and procedures are described in the literature.

#### CONCLUSIONS

We wish to offer some perhaps abrupt statements which may seem too fanciful, but which may at least lead surgical thought toward the solution of some of the hitherto insoluble problems in the field of disease. All observers should certainly stop, look and listen where so little is known and where there is so much to be learned.

*What is unknown of regional ileitis?*

1. Its causation is no further understood than at the time of the first report.
2. Is it bacillary?
3. Is it due to a parasite as some form of *ameba*?
4. Is it due to some worm?
5. Is it due to a fungus?
6. Is it due to chemical or mechanical irritation?
7. Is it due to a spirochete?
8. Is it due to micro-organism, one of the bacteria, or to an ultramicroscopic virus?
9. Why so little progress until the present?

*Undoubtedly the known facts are:*

1. A peculiar disease of the small bowel and colon.
2. It affects most often young males.
3. It may be acute or chronic.
4. It involves most frequently the terminal ileum.
5. It causes narrowing of the lumen and stenosis.
6. It may produce ulceration, the formation of adhesions, fistulae, and abscess formation.
7. It produces lassitude, anemia, loss of flesh and strength.
8. The pathologic picture is similar to but not identical with that in inflammatory conditions.
9. There is present the formation of new tissue and in this it resembles interstitial tuberculosis, lues, and malignant disease, and like the latter may result in ulceration.
10. Its granuloma grossly resembles that seen in tuberculosis, blastomycetes, and other mycotic lesions, lymphadenoma, Hodgkin's disease, sarcoma and carcinoma. The microscopic pictures differ in these conditions so that a competent pathologist can as a rule differentiate the exact lesion by a study of the history, the gross and the microscopic structure of the tissue.

A number of diseases formerly grouped as cancers, by the studies in pathology and by investigations as to causation, have been removed from such grouping and their true nature, their causation, their symptoms, their pathology and their curative treatment placed on a firm scientific basis. Is it not possible that the intensive study of ileitis, the causes and pathology of which are not known, may show the way more clearly to the discovery of the causes of cancer, sarcoma, Hodgkin's disease, lymphosarcoma, leucemia and other forms of anemia? All these conditions are obscure in their causation and their early development.

#### REFERENCES

1. BARBOUR, R. F., and STOKES, A. B. *Lancet*, 1: 299, 1936.
2. BRAUN, H. *Arch. f. klin. Chir.*, 13: 378, 1901.
3. BRAUN, H. *Deutsche Ztschr. f. Chir.*, 100: 1, 1909.
4. CROHN, B. B., GINZBURG, L., and OPPENHEIMER, G. D. *J. A. M. A.*, 99: 1323, 1932.
5. ERB, I. H., and FARMER, A. W. *Surg., Gynec. & Obst.*, 61: 6, 1935.
6. KANTOR, J. L. *J. A. M. A.*, 103: 2016, 1934.
7. MIXTER, C. G. *Ann. Surg.*, 102: 674, 1935.
8. MOYNIHAN, B. G. A. *Edinburgh M. J.*, 63: 228, 1907.
9. PEMBERTON, J. J., and BROWN, P. W. *Ann. Surg.*, 105: 855, 1937.
10. PEMBERTON, J. J., and WHITTAKER, L. D. *Surg., Gynec. & Obst.*, 65: 92, 1937.
11. SPROULL, J. *Am. J. Roentgenol.*, 36: 910, 1936.
12. TIETZE. Crohn's article. *Ergebn. d. Chir. u. Orthop.*, 12: 211, 1920.



# SURGICAL REMOVAL OF LARGE RETROPERITONEAL SACROLUMBAR GANGLIONEUROMA

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ALTHOUGH Loretz<sup>1</sup> in 1870 was the first to describe a well authenticated case of ganglioneuroma, it was not until 1898 that the first case of a ganglioneuroma located in the pelvis appeared in the literature. In that year Busse<sup>2</sup> reported a case of a retroperitoneal tumor in the pelvis weighing 700 Gm., found in a boy 4 years of age. The following year Cripps and Williamson<sup>3</sup> reported one in a young woman 21 years of age in which an operation was performed successfully. Since then ganglioneuromas located in the pelvis have been reported by Chiari,<sup>4</sup> Beneke,<sup>5</sup> Braun,<sup>6</sup> Schorr,<sup>7</sup> Kehrer,<sup>8</sup> and others.

In 1931, McFarland<sup>9</sup> reviewed the literature and collected only ninety-three cases of ganglioneuromas. These he grouped as to their location found on the body.

It is probable that these tumors are much more common than the review of the literature would indicate. They are seldom diagnosed before operation, and at times after operation they are diagnosed fibromas or fibrosarcomas, which they so closely resemble.

Although the term neuroma was first used by Odier<sup>10</sup> in 1803, it was loosely applied to any tumor related to a nerve. It was not until 1863 that Virchow<sup>11</sup> placed the pathology of neuromas on a histologic rather than on a clinical basis. He classified neuromas into true and false neuromas (pseudoneuroma). The true neuroma is derived from specific nerve tissue, being the result of hyperplasia of ganglia. It consists principally of medullary and nonmedullary nerve fibers and of ganglion cells. False neuromas arise from the connective tissue of nerves or the sheath of Schwann and are fibromas, sarcomas, neurinomas, or some other tumors.

It was, however, Pick and Bielschowsky<sup>12</sup> in 1911, who first revealed the close relationship between ganglioneuromas and the sympathetic nerve elements, and classified true neuromas on an embryonic basis. They named them embryonic sympathetic gangliomata. They emphasized the fact that neuromas consisted of nerve cells, originating either from the sympathetic nervous system or the cerebrospinal nerves and ganglia. When the ganglions were in abundance, the tumor was called a ganglioneuroma, and when considerable mixture with glia was present, a ganglioglianeuroma.

These tumors are now considered to develop at the site of cell nests that had become misplaced or miscarried during migration of the ganglionic crests during embryonic life, and, therefore, are congenital in origin.

By the degree of differentiation of these misplaced cells mature or benign and immature or malignant forms of neuroma may occur.

The gross picture of a ganglioneuroma is that of a moderately firm, elastic, nodular tumor which varies from the size of a pea to that of a man's head. It possesses a distinct but ragged capsule which retracts when incised, causing an eversion of the incised edge. Sectioning usually reveals a glistening, translucent, pale yellowish pink tissue in which septa of connective tissue divide the cut surface into relatively large lobules. These fine trabeculae course through the tumor much as they do in a fibromyoma.

The microscopic picture is quite characteristic. Both nerve and connective tissue are present. One can see bundles of nerve fibers in longitudinal and transverse sec-



tions lodged within by a connective tissue stroma. Numerous ganglion cells, singly or in groups, occasionally with naked axis cylinders, are prominent. They may be large, globular, unipolar or multipolar. The cytoplasm is slightly granular and usually contains tigroid substance. Extending from the cell body one or more processes may be found. The deeply staining nuclei are usually round and contain fine small granules, and a fine distinct nuclear membrane. Often a nucleolus is present. Occasionally the cells are multinucleated. The stroma in some areas is dense, in others, loose and fine. It consists of numerous neurofibrils which may be brought out by special staining methods. Areas of degeneration and even calcification may be present in the tumor.

Ganglioneuromas have been located in all parts of the body, but they are most prominent in the retroperitoneal spaces of the thorax and abdomen. They have been found in the brain (Schmincke,<sup>13</sup> Courville<sup>14</sup>), in the Gasserian ganglion (Risel<sup>15</sup>), in the appendix (Oberndorfer,<sup>16</sup> Lichtenstein and Ragins<sup>17</sup>), in the intestines (Poate and Inglis<sup>18</sup>), and even in the knee (Hagenback<sup>19</sup>).

The tumor, as a rule, is solitary. However, Kredel and Beneke's<sup>20</sup> patient had 160 and Knauss'<sup>21</sup> patient sixty tumors. It is slightly more frequent in women than men, more on the left side of the body than the right, and more prominent in the first twenty years of life. The oldest patient in which the case was reported was in a man 76 years old (Weichselbaum<sup>22</sup>).

The tumors tend to be of fairly large size, especially in the younger individuals. Yet, the more benign the tumor, the more advanced the age incidence. That these tumors may become malignant is well demonstrated in the cases of Kredel and Beneke,<sup>20</sup> Martius,<sup>23</sup> and Jacobsthal.<sup>24</sup>

The symptoms are variable and may be entirely absent if the tumor develops in locations where no symptoms may be produced, and under such circumstances it is often an accidental finding at autopsy

when the patient had died of some other disease.<sup>25</sup> Occasionally a tumor may give rise to symptoms for a short or long period of time, by displacement or pressure on the neighboring organs and nerves. Bigler and Hoyne's<sup>25</sup> first case is a good example of this. The tumor was located in the mediastinum, causing displacement and compression of the trachea with the clinical picture of a laryngeal or tracheal obstruction. In Williamson's case, the tumor which was located on the sacrum caused dysmenorrhea and at the same time displaced and anteflexed the uterus.

The prognosis is usually good. The majority of the tumors are benign, and harmful only because of pressure upon the surrounding vital structures. These tumors are slow growing and have been known to have been present for years and have little or no tendency to become malignant. However, the prognosis is best in all operable cases even though there is microscopic evidence of early formative cells (undifferentiated or immature cells). Up to the year 1931, thirty-nine cases had been operated on with only five deaths.

As to treatment, surgical removal seems to be the only cure. Roentgen ray therapy has been tried without noticeable results (Sommerfelt<sup>26</sup>).

#### CASE REPORT

R. K., a married woman, aged 25 years, a registered nurse, had been perfectly well up to January, 1936, when she began to complain of progressive loss in weight, nervousness, and constipation. She sought medical attention and was advised by her doctor to have her tonsils removed. In April, 1936 she had a tonsillectomy performed. This was followed by a further loss in weight down to 94 pounds. A bilateral neuritis of the upper extremities was present to January, 1937. A roentgenogram of the chest taken during this period was found to be normal. The patient then apparently began to improve in strength and gained weight until October, 1937. At this time she noticed a constant lumbosacral backache that progressively grew worse, that was not relieved by rest in bed and applications of heat, that was not

associated with menstrual periods, and that made the patient resort, at times, to sedatives in order to obtain some sleep. She described

There was a slight lumbar kyphosis of the spine, but no shortening of either leg. There was slight tenderness in the epigastric region on



FIG. 1. Gross appearance of the tumor.

the constant pain as dull and dragging, non-radiating, with occasional exacerbations. Although the patient had been constipated for years, she had not resorted to enemas or cathartics until the last few months in order to have a bowel movement. She also noticed during these last few months a heavy sensation in the rectum on attempting to have a bowel movement.

The first week in January, 1938 she noticed that she was having tarry stools unassociated with any gastrointestinal complaints except excessive eructation and progressive constipation.

Her past history revealed that she had had the usual diseases of childhood—whooping cough, measles, scarlet fever, chickenpox, and mumps. She also had had a severe case of anterior poliomyelitis at the age of 3 which kept her in bed for six weeks. Tenectomy operations were performed on her right leg when she was 7, and on her left leg when she was 10. She started to menstruate when she was 17 years old. Her periods had been regular every twenty-eight days, lasting three or four days, with moderate bleeding, always associated with severe dysmenorrhea and premenstrual pain in the breasts. The premenstrual pain was distinct and separate from the pain noticed in the sacrolumbar region. Although married three years, the patient had made no attempt to become pregnant. Her family history was essentially negative. There was no history of cancer or tuberculosis in the family.

deep palpation. A firm hard rounded mass was palpable just above the pubic symphysis, apparently extending into the pelvis. The liver, kidneys, and spleen were not palpable. Vaginal examination revealed a long conical cervix that was displaced forward and upward, pointing almost at right angles to the right side. A firm nodular mass, the size of a four months pregnancy, appeared to fill the pelvis, more prominent on the right than on the left. Bimanually, the uterus was found to be markedly anteflexed immediately behind and to the left of the symphysis pubis. It appeared infantile in size and could be easily moved away from the mass. Rectal examination revealed the mass to be adherent to the sacrum and lumbar regions. The coccyx was free and not attached to this mass. The bowel appeared to be displaced to the left but moved freely over it. Bimanually, it was possible to move the tumor slightly out of the pelvis for a distance of  $\frac{1}{2}$  to  $\frac{3}{4}$  of an inch by exerting pressure through the posterior wall of the vagina.

Roentgen ray examinations of the stomach, duodenum, small bowel and colon, including a barium enema proved essentially normal. Roentgenograms of the spine and pelvis revealed a lumbar sacral kyphosis of the spine and an indefinite shadow in the pelvis corresponding to the palpable tumor mass. An Ewald test revealed a total acidity of 64, and a free HCl of 38. Repeated stool examinations showed no macroscopic but positive chemical

(benzidine) evidence of blood. Examination of the blood showed 4,400,000 red cells, 9,000 white cells, and 80 per cent hemoglobin. There

incision, the patient became very pale, the pulse became very faint and over 172 per minute, and the blood pressure dropped to a systolic of



FIG. 2. Section of tumor revealing numerous ganglion cells scattered throughout. The numerous round nuclei are oligodendrocytes, the fibers are mostly nerve axones; the dark round cell bodies are ganglion cells (Bielschowsky stain;  $\times 125$ .)

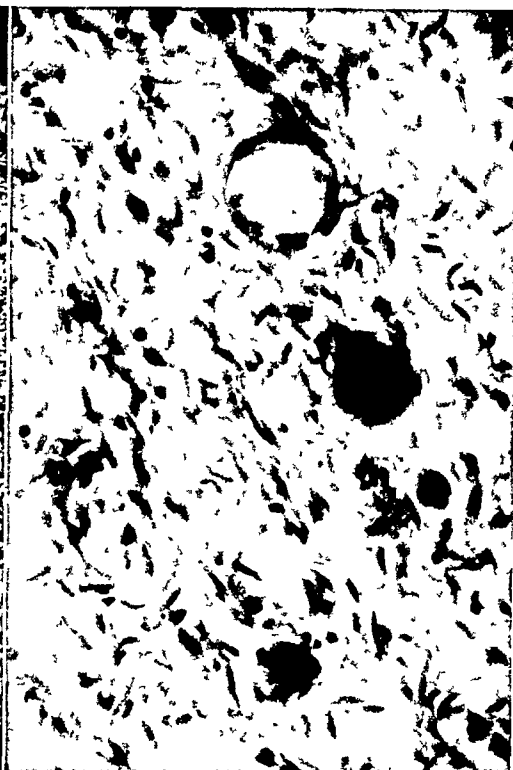


FIG. 3. Section of tumor revealing several ganglion cells with distinct nuclear membranes, surrounded by a variety of cells. The round nuclei are oligodendrocytes, the oblong are Schwann cells (Crystal violet stain;  $\times 500$ .)

was a lymphocytosis of 67 per cent. The urine was normal and the Wassermann test negative.

The mass was considered as probably an ovarian tumor or a retroperitoneal or broad ligament fibroma.

Through a lower midline incision with the patient in the Trendelenburg position, an exploratory operation was performed. The uterus was small, anteflexed and displaced to the left. The tubes, ovaries and broad ligament were healthy. The tumor was found behind the uterus, retroperitoneal and in front of the sacrum. The posterior parietal peritoneum was incised. An attempt to shell out the tumor with the fingers was successful. Separation from the peritoneum was easy, but some difficulty was noted in separating with the fingers the firm attachments between the mass and the anterior aspect of the sacrum.

Immediately after the tumor was removed, with some difficulty, through the abdominal

60 mm. The stomach was seen to dilate very rapidly, with the greater curvature appearing at the wound. To combat the severe shock, the anesthetic was stopped and the patient was given immediately  $\text{CO}_2$  and  $\text{O}_2$  inhalations, and 1 c.c. of adrenalin and 1 c.c. of coramine solution. Intravenously glucose, five per cent solution, was given freely. Because the patient responded poorly to the stimulants, the cavity was immediately packed with sterile gauze and the wound rapidly closed in layers.

The patient remained in severe shock for several hours with respirations at times six to eight per minute. She had a stormy course for several days with abdominal distention and lower sacral pain, but was up and around and completely free of pain in two weeks when she went home.

The tumor (Fig. 1) measured  $7.5 \times 12 \times 14$  cm. and weighed 600 Gm. The specimen was ovoid in shape, slightly lobulated, and

covered by a ragged, thin but firm capsule. The knife cut it with a grating sound. The tissue appeared firm and elastic and did not contain any visible blood vessels. The cut surface revealed a glistening pale yellowish pink, tissue.

On microscopic examination the tissue proved to be mainly neurogenic. A specimen was submitted to Dr. G. B. Hassin, Professor of Neurology at the University of Illinois. Through his cooperation we are able to submit his report on the microscopic picture:

"The tumor mass consists of ganglion cells (Fig. 2) and numerous nerve fibers devoid of myelin but supplied with well developed Schwann cells. (Fig. 3.) The Schwann cells are predominating elements in the field of vision, appearing in the form of oblong, darkly stained nuclei (especially well seen in the silver stained specimens). Other cell bodies are represented by round nuclei, the size of lymphocytes, which they much resemble, and are so called glia nuclei or oligodendrocytes. It is also possible to make out oval pale nuclei which belong to the endoneurial connective tissue membranes of the nerve fibers. Some areas exhibit quite numerous ganglion cells in the form of round bodies, their nuclei situated at the periphery and their cytoplasm homogenous or slightly granular often containing pigment. In their appearance the ganglion cells are similar to those seen in the sympathetic nervous system. The axones of the nerve fibers (Figs. 2 and 4) are often spindle shaped, varicose, sometimes quite thick and deeply stained, but in the majority of instances are as thin fibers lined by Schwann cells which in their turn are enveloped by an endoneurial membrane. The fibers so numerous over the visual field are connective tissue, others—the majority—are glial."

The diagnosis was ganglioneuroma.

The patient was given 250 units of antuitrin-s several months later, the substance being given twice a week for three months. The uterus became normal in size and the patient subsequently became pregnant. A 6 pound female infant was delivered December 2, 1939 by cesarean section. Both mother and child are in excellent health.

#### SUMMARY

A case of retroperitoneal sacrolumbar ganglioneuroma in a young woman is reported.

Ganglioneuromas are now considered tumors of congenital origin, arising from the differentiation of misplaced multi-



FIG. 4. Note large ganglion with distinct peripheral nucleus, with granular cytoplasm and deeply staining axone. (Bielschowsky stain;  $\times 368$ .)

potential embryonic neurocytes. These tumors may be present in any region of the body, but the majority have been located in the retroperitoneal spaces of the thorax and abdomen.

The only cure is surgical removal.

Profound serious surgical shock should be anticipated with the removal of large ganglioneuromas.

#### REFERENCES

1. LORETZ, W. Ein Fall von Gangliosem (Gangliom). *Virchows Arch. f. path. Anat.*, 49: 435, 1870.
2. BUSSE, A. Ein grosses Neuroma Gangliocellulare des Nervus sympathicus. *Virchows Arch. f. path. Anat., Suppl.* 151: 66, 1898.
3. CRIPPS, H., and WILLIAMSON, H. Retroperitoneal tumor connected with the sacral plexus. *Brit. M. J.*, 2: 10, 1899.
4. CHIARI. Discussion on Beneke's communication. *Verhandl. d. deutsch. path. Gesell.*, 1898.

5. BENEKE. Zwei Fälle von Ganglioneurom. *Beitr. z. path. Anat. u. z. allg. Path.*, 30: 1, 1901.
6. BRAUN. Ueber Ganglioneurome. *Arch. f. klin. Chir.*, 86: 707, 1908.
7. SCHORR, G. W. Ganglioneurom des peripherischen Nervensystems. *Zentralbl. f. allg. Path. u. path. Anat.*, 23: 91, 1912.
8. KEHRER, E. Retroperitoneal ganglioneuroma in pelvis. *Arch. f. Gynäk.*, 158: 582, 1934.
9. MCFARLAND, J. Ganglioneuroma of retroperitoneal origin. *Arch. Path.*, 11: 118, 1931.
10. ODIER. Cited by Wahl, H. R. *J. M. Research*, 30: 205, 1914.
11. VIRCHOW, R. *Virchows Arch. f. path. Anat.*, 13: 256, 1858.
12. PICK, L., and BIELSCHOWSKY, M. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 6: 392, 1911.
13. SCHMINCKE, A. Beitrag zur Lehre der Ganglioneurome. *Beitr. z. path. Anat. u. z. allg. Path.*, 47: 354, 1910.
14. COURVILLE, C. B. *Arch. neurol. u. Psychiat.*, 24: 439, 1930.
15. RISEL. Ueber multiple Ganglioneurome der Gasser'sche Ganglien und der Hirnnerven. *Verbandl. d. deutsch path. Gesel.*, 13: 341, 1909.
16. OBERNDORFER. Beitrage zur Frage der Ganglioneurome. *Beitr. z. path. Anat. u. allg. Path.*, 41: 269, 1907.
17. LICHTENSTEIN, B. W., and RAGINS, A. B. Ganglioneuroma of the vermiform appendix. *Arch. Path.*, 24: 786, 1937.
18. POATE, H., and INGLIS, K. Ganglioneuromatosis of the alimentary tract. *Brit. J. Surg.*, 16: 221, 1928.
19. HAGENBACH, E. Ueber ein Ganglioneurom der Kniegelenksgegend. *Deutsche Ztschr. f. Chir.*, 99: 570, 1909.
20. KREDEL and BENEKE. *Deutsche Ztschr. f. Chir.*, 67: 239, 1902.
21. KNAUSS. *Zentralbl. f. allg. Path. u. path. Anat.*, 22: 684, 1911.
22. WEICHSELBAUM. *Virchows Arch. f. path. Anat.*, 85: 554, 1881.
23. MARTIUS, K. *Ztschr. f. Path.*, 12: 442, 1913.
24. JACOBSTHAL. *Verbandl. d. deutsch. path. Gesel.*, 13: 343, 1909.
25. BIGLER, J. A., and HOYNE, A. *Am. J. Dis. Child.*, 43: 1532, 1932.
26. SOMMERFELT, L. Ein Fall von Ganglioneuron am Hals. *Zentralbl. f. allg. Path. u. path. Anat.*, 30: 641, 1920.



# CALCIFYING TENDINITIS TRAUMATICA

## DIAGNOSIS AND TREATMENT OF POST-TRAUMATIC CHANGES IN AND ABOUT JOINTS

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IN a previous publication the author<sup>1</sup> reported a case of tendinitis ossificans traumatica. A review of the literature was made at that time and the theories of heterotopic bone formation were discussed. Since that publication many excellent case reports and clinical observations of similar nature have been made. The purpose of this paper is to report three cases of calcification resulting from injury to tendon and ligamentous tissue involving the elbow, knee, and shoulder. It is very likely that ossification often results from or is preceded by calcification. In this manner heterotopic bone formation may occur.

A mass of evidence is accumulating which indicates that para-articular calcification is a frequent result, both early and late, of trauma in and about the joints. The pathologist recognizes this as one of the results of tissue disintegration and repair. By understanding the pathologic changes the orthopedist is better able to arrive at the proper method of treatment. Callen,<sup>2</sup> in an excellent article on Pellegrini-Stieda's disease, draws the conclusion that this particular condition is not a disease entity but represents a local manifestation in the knee of post-traumatic changes common to other joints. Three case reports are herewith presented. In the writer's opinion, each presents evidence that Callen's conclusion is justified.

### CASE REPORTS

CASE I. B. H., female, age 29, was admitted to the Miami Valley Hospital on December 20, 1935, with a chief complaint of swelling and tenderness about the left elbow. Moderately severe trauma to this joint had occurred three months before admission, but there were no symptoms in the interim. Four days previous

to admission swelling with pain again appeared, this time without any associated trauma, and became progressively worse. Aspiration had proved unsuccessful.

Examination of the elbow revealed a lemon-sized, non-fluctuant swelling, with a dully inflammatory reaction over the external condyle. This swelling was exquisitely tender. Motion was painless between 45 and 130 degrees. Beyond these limits motion was restricted by pain. Pronation and supination were free. There was no physical or mensurable atrophy. The temperature was 98.6°F. The remainder of the general physical examination was not significant.

Urinalysis showed nothing of significance. The red blood cell count was 4,000,000; the white blood cell count was 7,700; hemoglobin was 76 per cent. Differential showed polymorphonuclear filaments 39, nonfilaments 35, lymphocytes 20 per cent, monocytes 4 per cent, eosinophiles 2 per cent. Sedimentation time was one hour, eleven minutes. The Roentgen examination showed an area of increased density about the external condyle. No significance of this shadow was recorded.

On December 21, due to the persistence and severity of symptoms, the region was explored. A thick, caseous, chalky abscess was encountered in the radial collateral portion of the joint capsule. The abscess was evacuated and the wound closed without drainage. Short wave diathermy was instituted after the joint was immobilized in plaster splints. The convalescence was uneventful and the patient has remained well. Smears and cultures made at the time of the operation revealed no micro-organisms.

The pathologic report of adjacent tissue showed that it was composed of broad bands of hyalinized fibrous tissue containing localized areas of lymphocytic infiltration and organizing inflammatory fibrosis. There was considerable reticulo-endothelial hyperplasia of many of the new formed blood vessels in the area of active

chronic inflammation. No evidence of tuberculosis or malignancy was reported.

CASE II. R. B., male, 16, was seen Novem-

A Shantz compression dressing was applied. After five days the dressing was removed, and the extremity was immobilized in a bivalved

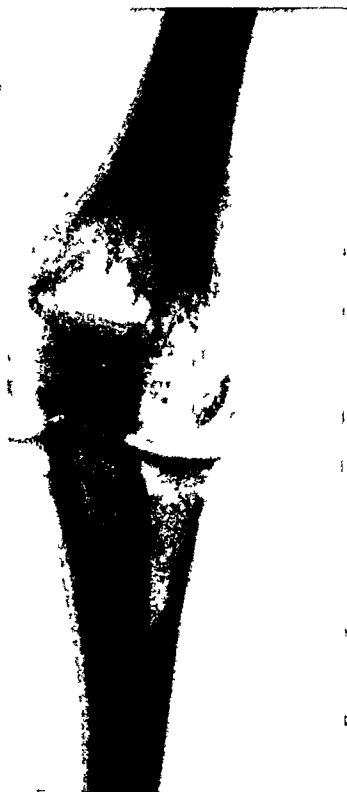


FIG. 1. Case I. An area of increased density in the joint capsule about the external condyle, without bony trabeculations, the result of trauma.



FIG. 2. Shadow removed and proved to be a calcified deposit.

ber 11, 1937 because of a painful, swollen left knee. Seven days previously he had been "tackled in football." The blow was received on the unprotected knee and the patient fell with the body weight landing on the lateral aspect of the knee. There was immediate disability with pain. Swelling was marked within the hour, and the knee had remained swollen. There was generalized tenderness and constant pain, particularly in the anterior and posterior thigh muscles.

Examination of the knee revealed swelling, marked effusion and generalized tenderness. Motion was limited in flexion to 110 degrees and in extension to 165 degrees. There was slight atrophy (1.5 cm.) of the thigh. Roentgen films showed area of increased density without bony trabeculations lateral to the external condyle. Aspiration yielded 150 c.c. of bloody exudate. A diagnosis of calcification in the capsule with hemarthrosis was made.

plaster cast. Diathermy was then instituted. Roentgen examination January 4, 1938 showed the complete absorption of the shadow. In eight weeks there was complete function with no complaints.

CASE III. H. S., male, age 51, complained of discomfort followed by pain in abduction of the right shoulder of three days' duration. Examination revealed deep tenderness over the great tuberosity of the right humerus. Abduction was limited by pain. Internal and external rotation were free. The patient was a dentist, and short wave diathermy was given for symptomatic relief to enable him to continue his professional duties for that day. Following one treatment, much of the distress was relieved and he desired to continue on this form of therapy. Treatments were given three times a week. In two weeks the patient was without symptoms. The area of calcification in the supraspinatus tendon was nearly absorbed.

As in Case III, these deposits have been shown by Codman<sup>3</sup> to be in the tendinous



FIG. 3. Case II. Area of density in joint capsule about external condyle of femur. Result of trauma.



FIG. 4. Complete absorption as result of conservative treatment.



FIG. 5. Case III. Calcified deposit in supraspinatus tendon.



FIG. 6. Same shadow after conservative treatment by short wave diathermy. Marked absorption had taken place.



insertion of the supraspinatus muscle or in the shoulder capsule, since these two structures are so intimately blended in the region of the trochanter. Mumford<sup>4</sup> has clearly shown some of the favorable results to be expected with diathermy. Here it was chronic occupational trauma rather than sudden injury that caused the joint manifestations.

#### COMMENTS

The exact process by which traumatized tendon fibers calcify and often later ossify has not been clearly demonstrated. Klotz<sup>5</sup> pointed out that calcium soaps may be an intermediate step between the fatty acids, a disintegration product, and the final calcium deposits. The chemical analyses of these deposits have not varied greatly in the reports of many writers. A physico-chemical process may occur, according to Karsner,<sup>6</sup> in which the necrotic material attracts calcium and the precipitation depends upon carbon dioxide concentration. The ready response to hyperemia with added nutrition to these devitalized tissues tends to show that the latter may be correct. Hyperemia induced by short wave diathermy has been shown in these case reports to result in an early absorption of the deposits. The pathologic findings in one

case revealed active chronic inflammation. There is nothing to justify the assumption that calcification would be the result of these cellular changes. With the rapid response to diathermy, fewer pathologic and chemical studies will be available.

#### CONCLUSIONS

1. Three cases of calcifying tendinitis are presented.
2. It is probable that the process in the three joints of different location are identical.
3. Recognition of the chemical and pathologic changes provides a good explanation for the favorable responses to conservative treatment.
4. In the type of heterotopic bone formation resulting from osteoblastic proliferation, surgical removal is usually necessary.

#### REFERENCES

1. BRUMBAUGH, H. L. Tendinitis ossificans traumatica. *J. Bone & Joint Surg.*, 14: 953-957, 1932.
2. CALLEN, H. S. Pellegrini-Stieda's Disease. A manifestation in the knee of post-traumatic changes common to other joints. *Radiology*, 29: 158-165, 1937.
3. CODMAN, E. A. *The Shoulder*. Boston, 1934.
4. MUMFORD, E. B. Calcified deposits in subdeltoid bursitis. *J. A. M. A.*, 97: 690-694 (Sept. 5) 1931.
5. KLOTZ, J. *Exper. Med.*, vol. 7, 1905.
6. KARSNER. *Human Pathology*. Philadelphia, 1926. J. B. Lippincott.



# CHONDROSARCOMA OF THE STERNUM\*

## REPORT OF A CASE

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**M**ALIGNANT cartilaginous tumors of the sternum are exceedingly rare. In 1932, Heuer<sup>1</sup> reviewed the primary cartilaginous growths, the rest being either sarcomata or metastatic malignancies. Thirty-four radical operations

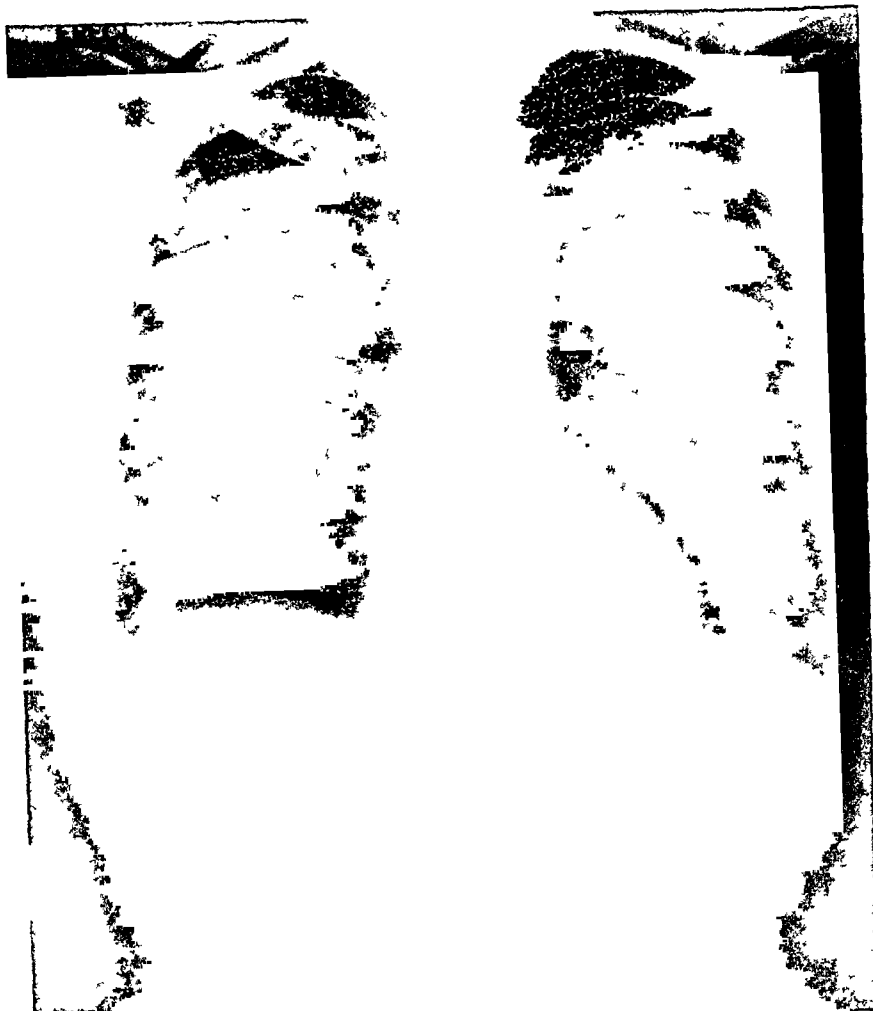


FIG. 1. X-ray taken March 1, 1938, showing soft tissue mass in superior mediastinum.

literature on neoplasms of the sternum and reported a case of chondromyxoma of the sternum, which, although histologically benign, gave rise to local and mediastinal metastases one year later. Heuer's case was the thirty-eighth reported malignancy of the sternum. Of these, only four were

were carried out in these thirty-eight cases and the immediate operative mortality was 23.5 per cent. Of the remaining twenty-three cases the end results were given in only thirteen. Nine of these showed recurrences within two years and six died in that time.

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Roberg<sup>2</sup> in 1935 reported a case of "chondroma" in a woman of 39. Radical resection of the upper sternum and ribs

Physical examination was negative except for the finding of a firm, fixed mass, about the size of a lemon, over the inner ends of both



FIG. 2. Photomicrograph ( $\times 100$ ) of section from margin of tumor. The growth is cellular and is made up of undifferentiated cartilage cells.

was carried out. The diagnosis histologically was chondroma with partial transition to sarcoma. Local recurrence and pulmonary metastases occurred within one year. This author stressed the uncertainty of character of primary cartilaginous tumors and the difficulty in determining the prognosis.

Because of the rarity of the condition we are reporting the following case of chondrosarcoma of the sternum.

#### CASE REPORT

M. B., female, aged 49, entered Jefferson Hospital on March 14, 1938 complaining of a mass over the upper end of the sternum. This had been present for four years, following a fall, and had been growing slowly since it first appeared. In 1935 a course of x-ray therapy was given, following which the mass remained stationary in size. In the previous year, however, the mass had again been growing slowly. There was no history of difficulty in breathing or swallowing. No cough or expectoration was present. Very occasional pains were noted in the suprasternal notch.

clavicles and the upper end of the sternum. X-ray examination on March 1, 1938 showed an indefinite soft tissue mass in the anterior portion of the superior mediastinum. The lung fields were clear.

On March 16, operation was performed under endotracheal cyclopropane-ether-oxygen anesthesia. A curved incision, with the concavity upward, was made across the upper sternum and the medial ends of both clavicles. The clavicular portions of the sternomastoid and pectoralis major muscles were separated from the manubrium and clavicles. A soft cystic swelling was encountered and a biopsy for frozen section taken. This was reported as suggestive of malignancy. Blunt dissection was then carried out behind the manubrium, separating the mass from the upper mediastinal structures. Openings were made in the second interspace on both sides and the pleurae and mediastinal structures separated from the posterior aspect of the sternum. The internal mammary arteries were ligated. The upper portion of the sternum, containing the mass, and the inner ends of both clavicles were then removed en bloc with a Gigli saw. The left pleural cavity was accidentally opened during the procedure. The opening was immediately

sutured. The incisions were closed, leaving one rubber drain under the skin. The pneumothorax was immediately aspirated. The patient left the operating room in good condition.

*Pathological Description.* The tumor was a firm, nodular mass which included the upper end of the sternum and the attached ends of both clavicles. The greater portion of the upper end of the sternum was replaced by a firm, nodular growth which had the appearance and consistency of cartilage. Some areas were very soft and hemorrhagic. The lower portion of the sternum appeared normal. No evidence of involvement of the clavicles could be demonstrated.

Microscopic sections showed largely cellular cartilage and fibrous tissue which formed distinct nodules. In some areas the cartilage cells were large, hyaline and adult in type but in other areas the bizarre type of nuclei suggested myxomatous tissue. The connective tissue stroma was very vascular in areas. Some nodules of cartilage could be observed in the attached muscle tissue.

While the greater portion of the growth was composed of cartilage, because of the cellular nature and the involvement of the surrounding tissues the lesion was considered malignant.

The diagnosis was chondrosarcoma of the sternum.

*Postoperative Course.* On March 18, 1938, x-ray of the chest showed evidence of a hydro-pneumothorax on the left side with displacement of the heart to the right. On March 19, a brace was applied to keep both shoulders from falling inward, because of lack of clavicular

support. A moderate degree of dyspnea and cyanosis developed and signs of a large collection of fluid in the left pleural cavity appeared. On March 28, stereoscopic x-rays of the chest revealed a density throughout the left chest with displacement of the heart to the right. On March 30, the left pleural cavity was tapped and 550 c.c. of serosanguinous fluid removed.

The hydrothorax gradually cleared up, although the convalescence was further complicated by bilateral femoral phlebitis. The patient was discharged with the wound well healed on May 3, 1938.

The patient was last seen at the beginning of February, 1940, twenty-three months after operation. The scar was well healed and there was no evidence of local recurrence. The brace had been discarded and there was no deformity and no impairment of motion of the arms.

#### SUMMARY

1. A case of chondrosarcoma of the sternum is reported.
2. The operative technique is described.
3. The fact that the inner ends of both clavicles were removed without any impairment of function is noted.

#### REFERENCES

1. HEUER, G. J. Tumors of the sternum; report of removal of a large mediastinal sternal chondromyxoma. *Ann. Surg.*, 96: 830, 1932.
2. ROBERG, O. T. Chondrosarcoma, the relation of structure and location to the clinical course. *Surg., Gynec. & Obst.*, 61: 68, 1935.



# CARCINOMA ORIGINATING IN AN OBSTRUCTING GASTRIC ULCER\*

## CASE REPORT

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**B**ECAUSE recent articles<sup>3,4</sup> have stated that gastric ulcers seldom if ever become malignant, we wish to submit

shows no evidence of healing, prompt surgical measures are indicated. Either an intractable gastric ulcer or an ulcerating



FIG. 1. Twenty-four hour roentgenogram showing almost complete gastric retention by an obstructing ulcerating pyloric lesion.

the following brief case report. We agree with MacCarty's many contributions<sup>1,5,6,7</sup> that a gastric ulcer should be viewed as a possible premalignant lesion and should be treated accordingly. All uncomplicated gastric ulcers must first be given an adequate trial under medical treatment in a hospital bed, for a period varying from six to eight weeks. If, after the expiration of that interval, epigastric abdominal distress still persists, or melena and hematemesis continue, or the gastric roentgenogram

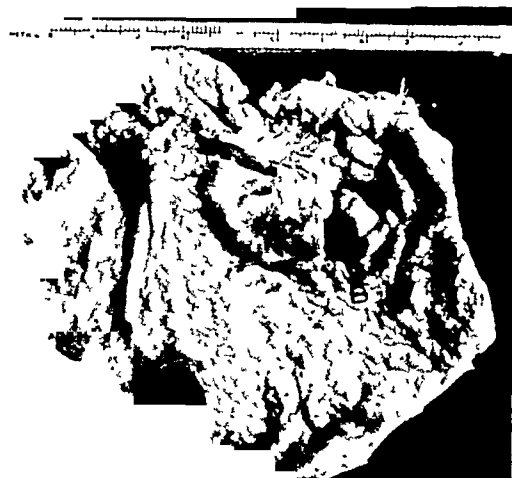


FIG. 2. Gross specimen, showing a large obstructing gastric ulcer near the pylorus. The ruler is placed at the pyloric end of the stomach. A, obstructed pylorus. B, site of the carcinomatous change originating from the margin of the ulcer.

gastric carcinoma is present, and medical measures will not suffice.

Five-year follow-up studies in unselected cases of gastric carcinoma, show that only 1 to 5 per cent of the original group remained alive. Thus, the only hope of saving more of these individuals must lie in the direction of earlier recognition and prompt treatment of the premalignant and early malignant lesions. Particularly valuable has been the contribution of Alvarez and MacCarty<sup>1</sup> basing the probability of malignancy on the diameter of the gastric lesion.

\* From the Departments of Surgery and Medicine and the Pathology Laboratory, Presbyterian Olmsted Memorial Hospital, Hollywood. Presented before the staff meeting of the hospital, September 27, 1938.

## CASE REPORT

Mrs. R. E., white housewife, aged 68 years, entered the Presbyterian Olmsted Memorial Hospital on September 10, 1938.

Abdominal exploration (Sloan incision) revealed an obstructing gastric lesion at the pylorus, about 3.5 cm. in diameter, situated on the anterior wall and involving the lesser

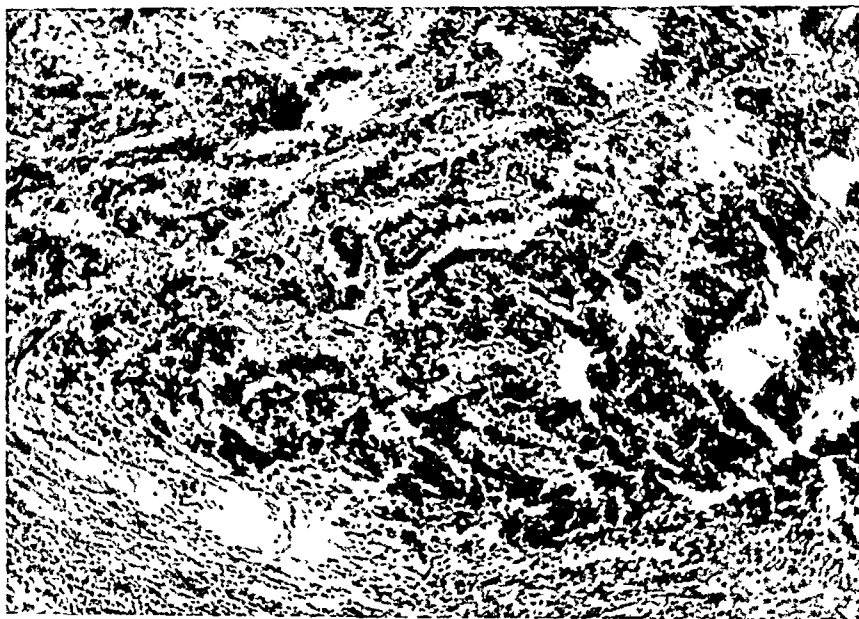


FIG. 3. H. and E. stain. Typical low power area of the carcinoma. Note lack of glandular formation. The protoplasm of the malignant cells stains a deep pink, indicating that possibly this neoplasm arose from the parietal cells of the stomach. ( $\times 100$ .)

She complained of inability to eat, weakness, anorexia, epigastric fullness and distress, which had begun about six months before.

She had taken some proprietary drugs for the relief of the vague abdominal distress, but it had gradually increased and was partially relieved by food. One month before admission anorexia and increasingly marked regurgitation of solid and then liquid foods, together with severe epigastric distress had occurred.

The patient weighed 115 pounds, having lost 9 pounds in six weeks. Blood pressure was 148/70. A small palpable mass in the right epigastrium was questionable.

Urine analysis was negative. The red cells numbered 4,000,000 per cu. mm., the white cells 6,350, with polymorphonuclears 54 per cent, lymphocytes 40 per cent, and monocytes 6 per cent. Hemoglobin was 66 per cent (Sahli). Coagulation time was  $3\frac{1}{2}$  minutes (Boggs).

Röntgenologic study of the stomach (by Dr. E. N. Liljedahl) revealed a practically complete twenty-four hour gastric retention of the barium meal by an obstructing ulcerating lesion at the pylorus. (Fig. 1.)

curvature. An exploratory gastrotomy with the palpating finger revealed a large obstructing gastric ulcer with one small area of marked firmness in its margin that extended toward the base of the ulcer. In view of these findings, and on account of the patient's advanced age, a posterior Polya-type gastric resection was performed, according to the Gray and Balfour technique.<sup>2</sup> Approximately 10 cm. of the distal portion of the stomach, including the pylorus and the proximal centimeter of the duodenum, was resected. (Fig. 2.)

The pathologic report (by Dr. V. L. Andrews) confirmed the large ulceration, which measured  $3\frac{1}{2}$  cm. in diameter and involved the inner part of the pyloric ring. For the most part the edges were elevated, slightly undermined. The base was quite smooth, as was the serous coat except for the manipulation of surgery. There was nothing indicative of malignancy on the serous coat.

Section through the base showed in the central part a small area of about 1 cm. a little firmer and with a pearly gray surface on the cut section. This could have been a beginning malignancy. Surrounding the ulcer and over

the inner surface of the stomach the mucosa was somewhat hypertrophied, but no other ulcerations were present.

2. We believe in the fundamental concepts of Wilson and MacCarty that gastric ulcers may become carcinomatous.

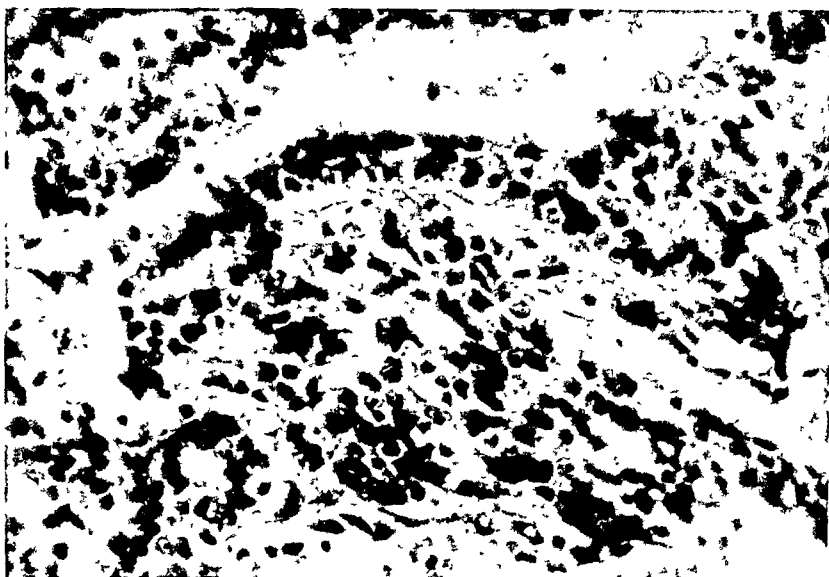


FIG. 4. H. and E. stain. High power appearance of a portion of the carcinoma. Cells show irregularity in size and shape with deep pyknosis of the nuclei. There are large collections of lymphocytes and plasma cells scattered throughout the neoplasm. ( $\times 440$ .)

Sections from two parts of the tumor showed a definite carcinomatous condition, with epithelial cells infiltrating in small groups and strands. They were irregular in size and shape but stained rather deeply. The protoplasm was pink and granular. There was no attempt at gland formation. An extensive lymphocytic infiltration was present throughout. Because there was no attempt at gland formation and the protoplasm was rather pink, the possibility that the tumor arose from parietal cells was considered. (Figs. 3 and 4.)

The temperature reached its peak of  $101.2^{\circ}\text{F}$ . per rectum on the first postoperative day and then rapidly subsided. The incision healed uneventfully. No nausea or vomiting occurred. The patient's convalescence was normal. She is now ready for hospital dismissal.

#### CONCLUSIONS

1. A case report of a proved carcinoma originating in an obstructing gastric ulcer is recorded, and its prompt surgical resection described.

3. We wish to stress, that despite recent contributions in the medical literature to the contrary, gastric ulcers are a definite premalignant lesion.

#### REFERENCES

1. ALVAREZ, W. C., and MACCARTY, W. C. Sizes of resected gastric ulcers and gastric carcinomas. *J. A. M. A.*, 91: 226-231 (July 28) 1928.
2. GRAY, H. K., and BALFOUR, D. C. Cancer of the stomach. *Am. J. Cancer*, 22: 249-286 (Oct.) 1934.
3. KLEIN, S. H. Origin of carcinoma in chronic gastric ulcer. *Arch. Surg.*, 37: 155-174 (July) 1938.
4. LAHEY, F. H. Peptic ulcer. *Pennsylvania M. J.*, 41: 79-85 (Nov.) 1937.
5. MACCARTY, W. C. Pathology and clinical significance of gastric ulcer. *Surg., Gynec., & Obst.*, 10: 449-462 (May) 1910.
6. MACCARTY, W. C., and BRODERS, A. C. Chronic gastric ulcer and its relation to gastric cancer. Review of 684 specimens. *Arch. Int. Med.*, 13: 208-223 (Feb.) 1914.
7. WILSON, L. B., and MACCARTY, W. C. The pathologic relationships of gastric ulcer and gastric carcinoma. *Am. J. M. Sc.*, 138: 846-852 (Dec.) 1909.

# NEW INSTRUMENTS

## ATRAUMATIC RETHREADABLE SURGICAL NEEDLES

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**S**TREAMLINING is the vogue of the day, to eliminate resistance and insure smooth performance. Why not make the operator. The needle is essentially the same now as when invented centuries ago: a sharp pointed shaft with an eye placed at

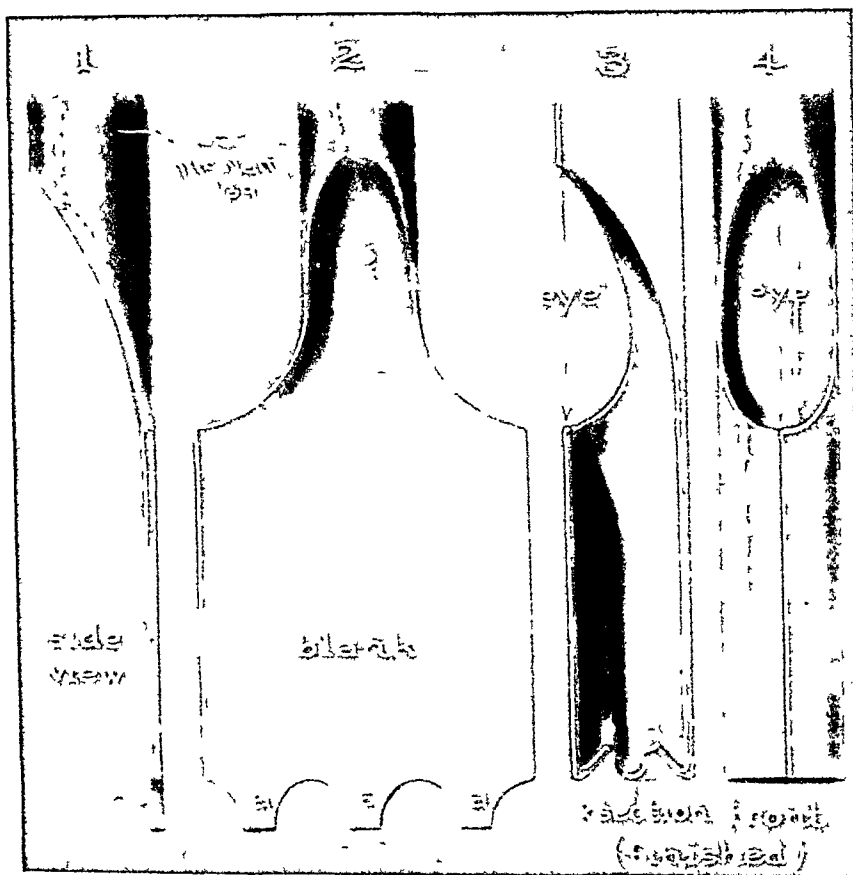


FIG. 1. Method of flattening, stamping and rolling blunt end of needle to form retaining unit for suture.

the principle applicable to surgical suturing? The sewing together of tissues is one of the oldest and most fundamental surgical procedures. The implements are the needle and the thread. The suture has many forms due to the needs and the whims of

the blunt end through which the suture passes at right angles to the shaft.

To avoid trauma and handle tissues with care is agreed to be the secret of successful surgery. A doubled piece of catgut plus the thickness of a needle can be an abrupt



sizable mass to pull forcibly through the tissues in the process of bringing these surfaces together.

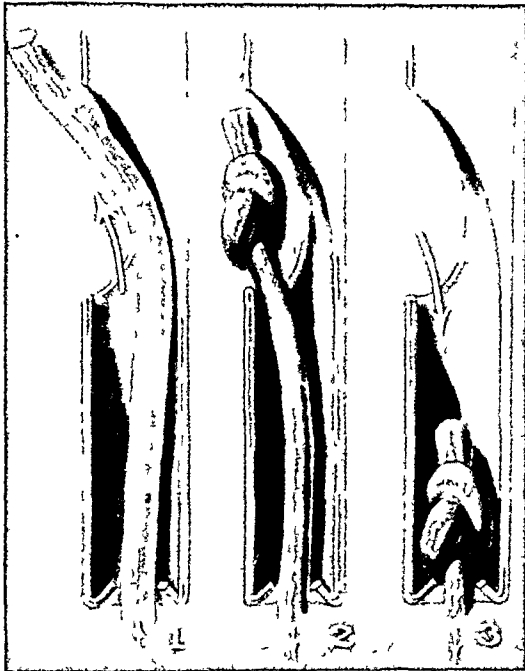


FIG. 2. Suture threaded into needle, tied into knot which is withdrawn inside needle.

We have seen frequent discussions of the relative value of various suture materials and the tissue reaction they produce. We might also concern ourselves with the tearing apart of fibrous tissue bundles, the separation of fasciculi of muscle cells, or the pulling apart of epithelial tissue masses. Small hematomas of varied significance no doubt result from this forcible separation of cellular elements. The increased pain from tissue pull in emergency suturing, where little or no anesthesia is used, should also cause consideration of the trauma caused by a doubled thread of suture material and the thickness of the needle. Often one has a needle carefully placed in the edges of a wound to approximate two delicate tissues, only to have the after-coming suture tear out as the thick doubled material is pulled through.

The atraumatic needle is already part of our armamentarium. But because most such needles are not easily rethreadable, they are not used routinely. A practical

rethreadable suture would doubtless lead to more widespread use of atraumatic needles, but it should be able to be manufactured by mass production rather than by hand and should also be easily handled, quickly threaded, with no loose parts to become misplaced or dropped. The two needles described here meet these requirements.

*Needle I.* (Fig. 1.) The rethreadable, retaining portion or eye of the needle is as usual at the blunt end of the shaft. The process of moulding this end is accomplished by flattening out the shaft for a short distance in the manner shown in Figure 1 (1 and 2). A blank is made in which the upper margins of the flattened surface curve inward to converge with the shaft of the needle. The other extremity of the flattened area has semicircular areas punched out, leaving three prong-like projections. (Fig. 1a.) This stamping is then rolled on itself so that the flattened area becomes cylindrical. The cylindrical portion is continuous with and of the same size as the body of the needle. The small projecting prongs are bent on themselves so that they are directed inward toward the lumen of the cylinder. The two curved areas at the upper portion of the cylinder fit together, forming the eye of the needle in the side of the shaft. (Fig. 1-3 and 4.) The needle is threaded easily by pushing the suture through the opening at its distal end. It comes out through the eye as indicated in Figure 2-1. A knot is then tied in the suture material, the redundant end cut off, and the suture withdrawn back into the shaft of the needle as indicated in Figure 2-3.

*Needle II.* (Fig. 3.) This needle is simply a modification of the previous one. Perhaps it will be more easily manufactured. The formation of a blank by the flattening out of the blunt end of the shaft is the same as that described in the previous example. However, rather than make projecting elements at the distal end, small prongs are formed in the flattened material as indicated in Figure 3b. These prongs are

bent inwardly. A cylinder is made as described in the previous Figures 1 and 2. The needle is threaded in the same manner

a wax, cellulose, or bakelite moulded swelling to be formed around the extreme end of the suture. A metal sleeve clamped

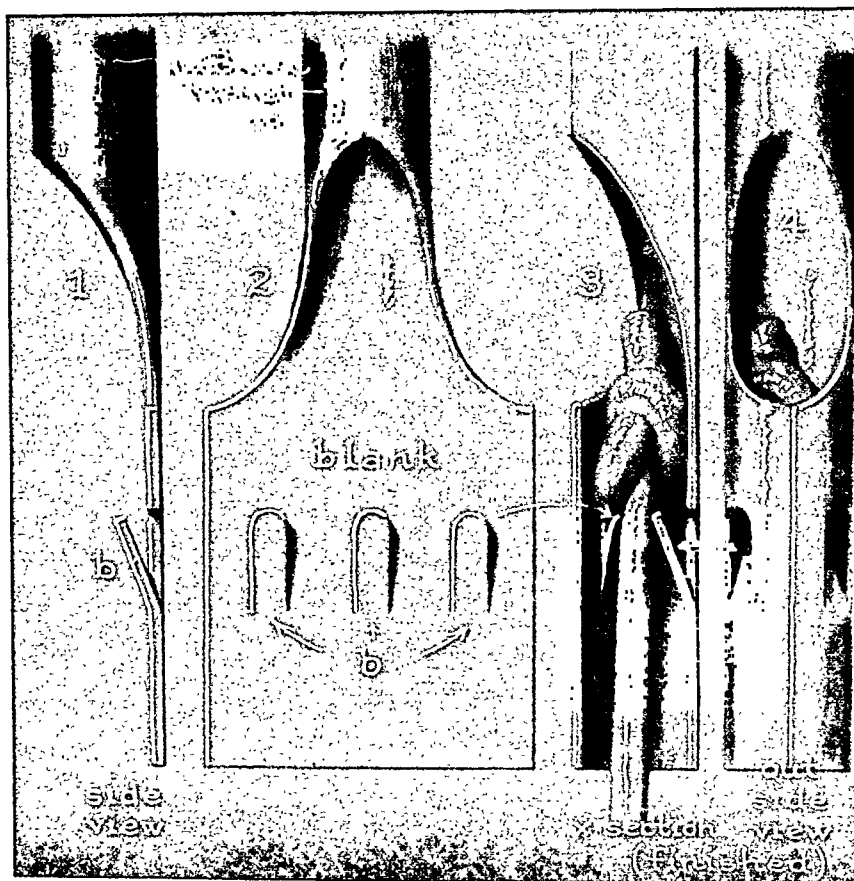


FIG. 3. Needle stamped with prongs inside of cylindrical end to hold suture in place.

with the drawing of the knot or other enlarged retaining device tightly against the flaps that have been bent inward from the sides of the cylinder. (Fig. 3-3 and 4.)

It will be noted that there is no sleeve or adjustment of locks that anchor the catgut into the needle as has been described by other writers.<sup>11</sup> The method of holding the catgut inside the needle is accomplished by the simple procedure of knotting the end. The knot can be displaced by a fine awl, forcing it back toward the open eye of the needle in the side of the shaft. Many other methods for enlarging the end of the suture have been suggested. The simple formation of a knot, however, is the oldest. Others consist of applying a hot cautery causing distortion of the end of a catgut suture. Logan, and later Everett, suggested

around the suture and then withdrawn into the shaft of the needle was also suggested by the latter writer.

The needle does not have any groove on the side from which the catgut can slip.<sup>2</sup> Nor does it clamp fast to the catgut so that the suture cannot be removed for rethreading (Bigelow, Gaillard, Ovington, Lukens, and Quint). The needle is rethreadable and simple to manufacture. Both of the needles have the strength at the blunt end or eye increased rather than decreased by the method of manufacture. The cylinder makes for more resistance than a single bar shaft.

#### CONCLUSION

There is a definite need for a practical atraumatic rethreadable needle. The ideas

for manufacture here presented are feasible and seem to solve the major difficulties.

#### REFERENCES

1. BIGELOW, JAMES. U. S. Patent 1,250,114. Dec., 1917.
2. EDWARDS, THOMAS. U. S. Patent 784,995. March, 1905.
3. EVERETT, SAMUEL. U. S. Patent 856,686. June, 1907.
4. GAILLARD, E. N. U. S. Patent 362,374. May, 1887. Original patent No. 149,034. March 31, 1874.
5. GRUSS, F. J. U. S. Patent 2,023,807. Dec., 1935.
6. LOGAN, O. J. U. S. Patent 1,981,651. Nov., 1934.
7. LUKENS, C. D. U. S. Patent 1,122,210. Dec., 1914.
8. MCCLURE, W. L. U. S. Patent 1,757,129. May, 1930.
9. OVINGTON, E. J. U. S. Patent 1,564,012. Dec., 1925.
10. QUINT, E. A. U. S. Patent 1,636,615. July, 1927.
11. SOUTTAR, H. S. U. S. Patent 1,613,206. Jan., 1927.
12. WATSON, JOHN. U. S. Patent 221,638. Nov., 1879.



HEMATURIA never should be treated as an ailment in itself but as a symptom of more serious trouble. The causes of hematuria are numerous, and its diagnosis and treatment do not belong to the realm of minor surgery.

# A RATIONAL SCALPEL\*

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THE correct use of the scalpel is one of the first technical principles learned by the surgeon. That the handle be held within restricted limits in order to sever tissue with the belly of the blade. Actually the scalpel can be held at angles

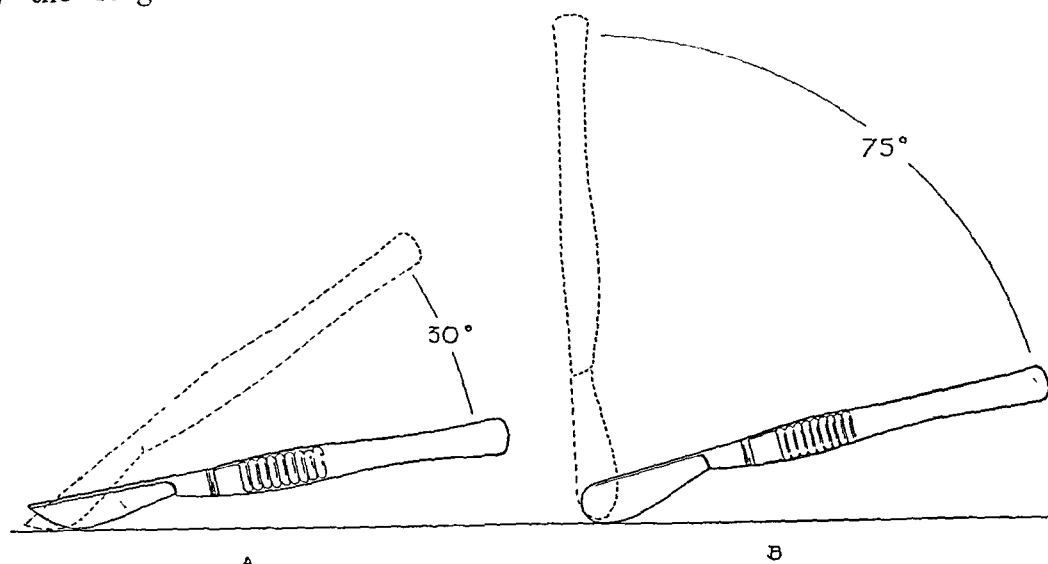


FIG. 1. Diagrammatic illustrations of A, conventional scalpel and B, type proposed. A, conventional scalpel which must be held at angles varying between approximately 15 degrees and 45 degrees in order to sever tissue with the belly of the blade. B, proposed scalpel with blade so shaped that the cutting edge forms an almost 180 degree curve at its end. Such a scalpel permits severance of tissue with belly of the blade at angles varying between approximately 15 degrees and 90 degrees with the surface to be cut.

should be held so that the cutting is done by the belly of the blade is common knowledge. Yet this surgical maxim is not generally realized. This becomes obvious upon considering the types of blade usually employed.

The scalpel most commonly used by the surgeon consists of the handle with a blade characterized by one of the two general forms of cutting edges: (1) the bistoury type in which the gradually tapering straight cutting edge forms a long sharply pointed blade; and (2) the belly type in which the sharpened edge follows a graceful curve to a relatively blunt point. The former is used in making stab incisions and the latter is employed for practically all other purposes. The obvious disadvantage of this latter type of scalpel is that it must

varying between approximately 15 degrees and 45 degrees with the surface to be cut. If the scalpel is held at an angle greater than 45 degrees, severance of tissue is no longer performed with the belly of the blade. Thus it permits variations of about 30 degrees. (Fig. 1A.) While this is not significant in the majority of instances where the knife can be used in open areas, it becomes a real objection in those cases where severance of tissue must be done through deep wounds. In the latter instance because the limited space does not permit the scalpel to be held at the proper angle with the surface to be cut, actual severance is usually performed with the tip of the cutting blade.

With this view in mind and in an attempt to obviate this objection, a scalpel

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has been devised which is considered more rational. The blade is so shaped that the cutting edge forms an almost 180 degree curve at its end. (Fig. 1B.) Such a scalpel permits severance of tissue with the belly of the blade at angles varying between

approximately 15 degrees and 90 degrees with the surface to be cut. (Fig. 1B.) The obvious advantage of this greater "bellied" blade is that it allows the surgeon to incise rationally at practically any angle it may be necessary to hold the scalpel.



FRACTURES involving sinuses are potentially the cause of infection which may proceed from the sinus itself to the adjacent soft parts. The rationale of the treatment is the reduction of the fractures and the protection of the sinuses, which is carried out by a rhinologist.

# OBSTETRIC DELIVERY FORCEPS

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**D**URING the conduct of an obstetrical delivery, a physician is confronted by a dual challenge. First, he must provide the parturient patient a method of safe, speedy and effective delivery of her offspring with a minimum of pain. And, secondly, he must give the child the guarantee of a life with a body and form free from any defects of the physician's making. In normal, spontaneous deliveries these challenges are easily met. However, in abnormal cases the hazards and challenges are great and success in handling of the cases is dependent not alone upon the knowledge and judgment of the physician attending, but upon the equipment at hand and dexterity in its management.

From earliest times, the obstetrical forceps has been one of the most effective agents, when properly used, of reducing both maternal and fetal mortality. Since obstetrical forceps were first introduced by the Chamberlen family in 1584, their use has increased, until in 1931 at the White House Conference it was reported by Plass<sup>2</sup> that, in a series of 145,812 deliveries, the incidence of forceps deliveries was 17.9 per cent.

In addition to the four main types of female pelvis, the gynecoid, the android, the anthropoid and the platypelloid (or flat) forms, as reported by Caldwell and Moloy,<sup>3</sup> there is a series of intermediate forms more difficult to recognize unless their anatomic relationship to the parent type is observed and recognized.

If the android and anthropoid pelvic type is recognized, the obstetrician may find that delivery can be effected with greater ease by delivery of the head with forceps in the persistent occipitoposterior position as compensatory space exists in the posterior pelvis. It is mechanically wrong to attempt

the rotation of the fetal head from a wide diameter through a narrow one. The same principle holds in the delivery of the after-coming head in a version and breech extraction. Therefore, it is logical to rotate the head to an occipitoposterior position in the inlet itself, if this is possible, in order to deliver the head in the occipitoposterior position.

With the forceps now in use, the difficulty is primarily that there is no chance for the head to rotate because of the tight grip which the operator has on the extremely rigid forceps handles. When traction is applied, the harder the operator pulls on the forceps, the harder he grips the handles. By so doing, he loses the sensation of the head within the blades which otherwise enables him to revolve the head to the larger and more favorable position within the pelvis in its descent.

The new forceps here presented resembles DeLee's modification of the Simpson forceps. It is just as easily applied and the blades are thinner; thus, it will occupy less space in the birth canal. The possibilities of free rotation with flexion and extension of the head, as well as the insertion of an elastic mechanism for the purpose of overcoming the friction of the head, is the goal sought. Consequently, this new forceps may well be considered entirely new in principle and design.

The swivel or ball joint bilaterally frees the head from any hindrance traceable to rotation, flexion or extension due to the pull of the physician. The head can gradually and fully turn automatically to conform with the diameters of the birth canal in spite of the direction of the pull exerted upon it. The rotation of the head is due to the pressure of the soft portions of the mother's body, especially posteriorly.

It is possible to prevent any hindrance to the free rotation, flexion or extension of the head by the use of the described forceps

are smaller than the head. The new blades are designed to fit the head and all curves are cephalic curves. The blades auto-

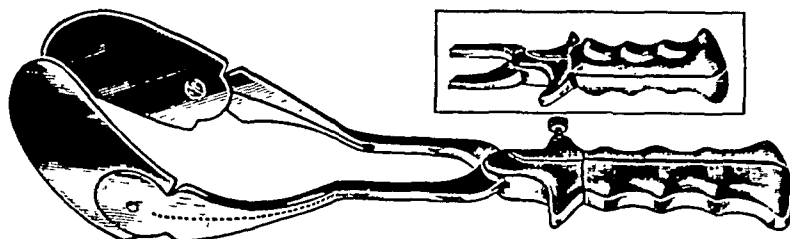


FIG. 1.

grip, thus enabling the replacement of natural labor powers by a forceps operation made to conform as closely as possible with natural conditions, and in a manner which might be considered entirely new.

The entire forceps is constructed as lightly as possible. This applies especially to the spoons, the thickness which is less than that of other forceps blades. This has been made possible by using solid blades.

The forceps has another advantage. It is especially equipped to manipulate one of the abnormal positions, occiput posterior position to occiput anterior position, or vice versa, when indicated. This is accomplished by rotating the head 180 degrees, if necessary, with one application. While this rotating movement is in progress, the blades automatically turn themselves to accommodate the new pelvic position, and also automatically adjust themselves to the pelvic curve. Delivery can be completed without removing or changing the first application of the forceps. De Lee,<sup>4</sup> using his own modification of Simpson's forceps, makes four different applications on the head to rotate 180 degrees.

A lock is provided in the shank to hold the forceps blades in a fixed position. This can be released by the operator after application of the forceps, thus allowing automatically free movement of the blades and the head during rotation and delivery.

It is unnecessary to provide blades with a pelvic curve in them since there is no pelvic curve in the head itself. There is no reason why the blades should be curved in the direction of the pelvic axis when they

automatically adjust themselves to the pelvic curve by the joint near the center, which assists the blades automatically to adjust themselves to the pelvic curve during the movement of rotating from the occiput posterior to occiput anterior position for delivery.

An obvious feature of the use of this new instrument is the fact that a second application of the forceps is not required during or after rotation has been completed.

#### CONCLUSIONS

The new forceps has the following advantages:

1. It is as easily applied as the Simpson forceps.
2. It is so constructed that when in place and locked, as traction is applied, the head is free to flex, extend or rotate to follow easily through the birth canal.
3. It facilitates the movement of the head along the longitudinal axis of the generative canal.
4. It reduces the pressure of the spoons to a minimum and equalizes the distribution of pressure in all parts of the birth canal during traction.
5. It eliminates the stiff bond between the head of the child and the hand of the physician since the head can extend, flex or swing as the pelvic curvature requires.
6. It is simply constructed, for safe manipulation and asepsis, but possesses axis traction advantages.
7. It requires but one application to rotate the head from an occiput posterior

position to an occiput anterior position (or vice versa), thus eliminating more chances of infection and trauma to mother and child.

8. It prevents the possibility of the head reverting back to its original position during the change of forceps.

9. The thumb screw on the right handle allows the operator to open or close the blades for a larger or smaller head.

10. The blades can be locked on the head by turning the outer handle right or left one-quarter turn.

11. The forceps blades can be locked in any desired pelvic curve before or during the application of the forceps. The locks can be easily released at the will of the operator.

The author wishes to express his gratitude to the following obstetricians who have accepted the new forceps for trial and given time and effort in the various stages of its development. Drs. Paul Titus, N. J. Eastman, John W. Harris, A. H. Lahmann, H. H. Cummings, J. B. DeLee, Fred L. Adair, William Dieckmann, R. M. Grier, William E. Caldwell, H. C. Maloy, Hugh J. Tunstead, A. B. Hunt, R. D. Mussey.

#### REFERENCES

1. GREENHILL, J. P. The Kielland Forcep. *Am. J. Obst. & Gynec.*, vol. 7, 1924.
2. PLASS, E. D. Relation of forceps and cesarean section to maternal and infant mortality. *Am. J. Obst. & Gynec.*, 22: 176, 1931.
3. CALDWELL, W. E., and MOLOY, H. C. *Am. J. Obst. & Gynec.*, 26: 479, 1933.
4. DELEE, J. B. *Principles and Practice of Obstetrics*, 7th ed. Philadelphia, Saunders.





# A STRETCHER SPLINT FOR SAFELY TRANSPORTING THE INJURED

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VERY important and yet almost universally inadequately managed is the problem of transporting the injured. It was several experiences with badly injured skiers on the mountain slopes that made the author realize the importance of

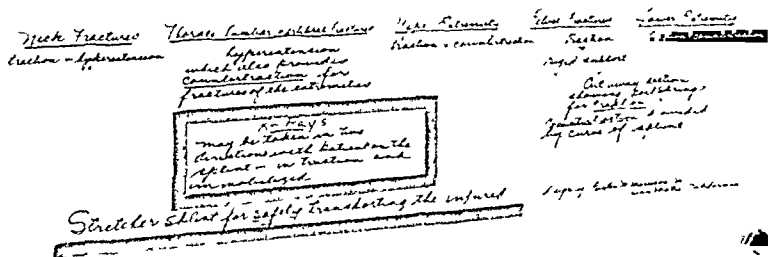


FIG. 1. Model of splint with wooden mannikin. Section cut away to show traction springs. Head sling is not necessary as dependent position supplies sufficient countertraction.

injured from the site of accident to the place of treatment. The damage done in transporting these injured people cannot be accurately estimated, but without doubt is considerable. Many people lose their lives through well meant but unskilled handling after injuries to bones and joints.

The football player who injures his neck and is carried off the field without protection of the cervical cord is sometimes dead by the time he reaches the side lines. Simple fractures are often compounded and traumatic shock is multiplied by ineffective means of immobilizing and protecting the injured during transportation. Serious added insult too often occurs between the ambulance and the x-ray table or even on the x-ray table.

these problems, and that confronted by major fractures in a person requiring transportation, his M.D. degree and ordinary facilities made very inadequate splints.

Present day equipment is far behind the present day accidents with their multiplicity of injuries and severe shocking power. The ordinary stretcher is helpful but inadequate, and when on extremely rare occasions a Thomas splint is available it is also helpful but in the hands of other than an expert may do harm and complicate handling. This equipment even if complete and available, as it very rarely is, provides little help in multiple injuries, and is especially inadequate in vertebral injuries.

In designing the stretcher splint here presented a hypothetical case of multiple injuries was considered, i.e., fractures of the vertebrae, pelvis, long bones of the arms and legs. The requisites for transporting each individual fracture problem were studied and a simple splint satisfying all requirements evolved.

A tabulation of these requirements follows:

1. *Vertebrae fractures and dislocations* (cervical, thoracic or lumbar): Immobilization with hyperextension, with or without traction.

2. *Pelvic fractures*: Rigid support with traction.

3. *Extremities* (long bones of arms and legs): Immobilization with traction and countertraction.

4. *X-rays*: Adequate two directional views should be possible without disturbing the patient.

5. *Multiple fractures*: These should be handled concurrently without extra equipment.

6. *Simplicity*: The apparatus should be "layman-proof."

All these requirements were found to be satisfied by the device.

The splint consists of a double plyboard frame about the size of a stretcher with the upper board gently arched and means of attaching traction to arms and legs.

The arched board provides hyperextension and thus gives protection for spinal injuries. This arch also provides a means of countertraction when traction is applied to ankles and wrists. Traction is made by long coil springs concealed between the boards which are so arranged that a pull of 10 pounds for legs and 5 pounds for arms is automatically obtained when the springs are attached to the extremities by Delbet knots or the Collins hitch.

It is also possible to apply head traction by using a chin occiput sling tied to the front of the splint. The splint can be placed on the x-ray table without disturbing the immobilization or traction and pictures taken by placing the films under or be-

tween the boards. A roentgenologist was consulted in designing this device and his enthusiastic approval was quite apparent.

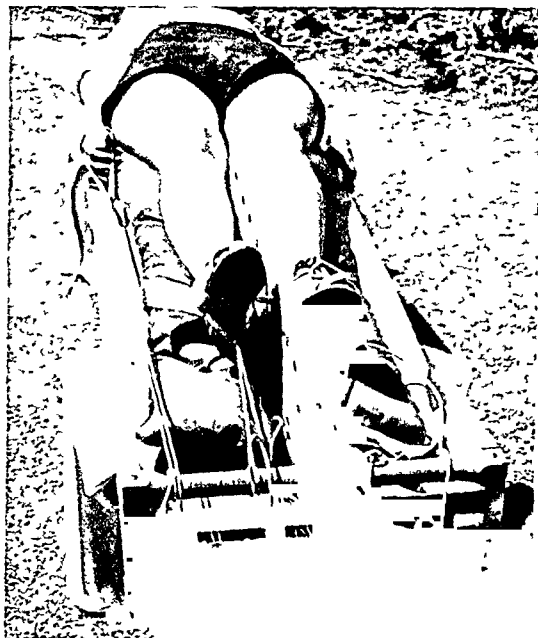


FIG. 2. Stretcher showing the manner of attaching traction to arms and legs. The ropes lead from springs between the body of the stretcher.

Use of the splint requires no diagnostic ability on the part of the ambulance attendant and instructions are simple. The patient is placed on his back on the stretcher which, by virtue of moderate hyperextension, protects the spinal cord and provides countertraction for the limbs. The ankle straps are applied and traction and countertraction thereby obtained. Rotation is prevented by tying the boot to the center spline. If there is injury to the upper extremity, the wrists can also be fastened to the traction mechanism. Thus by placing the patient on this stretcher in a certain easily learned manner, practically any fracture is immobilized and put in adequate traction and countertraction. Transportation hazards are minimized, x-rays are taken without difficulty and the vital spinal cord is protected.

#### SUMMARY

A stretcher for transporting the injured is described which in an almost automatic

fashion immobilizes and places in controlled traction and countertraction any long bone fracture. At the same time vertebral fractures are placed in sufficient hypertension to protect the cord and prevent increase in deformity.

There is no necessity for the first aid crew to make a diagnosis as there is only one way to position the patient regardless of the injury.

X-rays may be taken without taking the patient out of the stretcher.



THE fundamental principle involved in the *treatment of fractures of the clavicle* is traction. In the absence of traction the pull of the pectoral and scapular muscles and the weight of the arm will drag the shoulder mesially and will cause overriding or upward or downward deformity of the fragments.

THE brief excerpts in this issue have been taken from "Minor Surgery" by Frederick Christopher (Saunders).



[From Fernelius' *Universa Medicina*, Geneva, 1679.]

# BOOKSHELF BROWSING

## THE HISTORY OF LINGUAL CANCER

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CANCER of the external parts of the body (skin, breast, external genitalia) is mentioned by the earliest medical writers, who recognized it as a definite disease entity. The first application of the term "cancer" (or rather the Greek "karkinoma") to malignant neoplasms is generally credited to the Hippocratic school, although this source is apocryphal. In any event, long usage of the term had already obscured its derivation by the time of Galen (A.D. 130-200), for he explained its probable origin by pointing out that "just as a crab's feet extend from every part of its body, so in this disease the veins are distended forming a similar figure." Paulus Aegineta (A.D. 625-690) commented further, "But some say cancer is so-called because it adheres like a crab." Medieval writers also referred to the origin of the term, and de Mondeville (A.D. 1260-1320) repeated these comparisons and added one of his own—that a cancer progresses "en rongeant" like the crab which walks backward and to the side as well as forward.

TONGUE CANCER IN THE MEDICAL  
LITERATURE PRIOR TO THE  
EIGHTEENTH CENTURY

The curious lack of specific mention of tongue cancer in the medical literature

prior to the seventeenth century has already been noted by others. Certain portions of the Ebers Papyrus (about 1500 B.C.) have been interpreted as including directions for the treatment of "eating ulcer" of the gums and "illness of the tongue," which may refer to cancer. This document written in hieratic script is concerned mainly with therapeutics, and various diseases are listed (without further description) and their remedies prescribed. In the few significant medical writings of the first thousand years of the Christian era, cancer in general is frequently, though rather vaguely, mentioned, but there is no direct reference to this disease as affecting the tongue. So far as is known, the first definite published report of a case of lingual cancer was made by an Englishman, Alexander Reade, in 1635.

At first glance it may seem remarkable that there should be so little mention of lingual cancer in the early medical literature, since today cancer of the tongue makes up between 2 and 3 per cent of all human cancer and is responsible for about 1 to 2 per cent of all cancer deaths. Butlin, among other writers, interpreted this negative historic evidence as indicating that cancer of the tongue was relatively rare until the beginning of the seventeenth century. D'Arcy Power, who was of a

similar opinion, commented that the characteristic symptoms of lingual cancer, and especially those of its late complications, would have insured its more frequent recognition had the disease been as common then as it is now. These and other writers have pointed out that several of the etiologic factors which are known to be of importance in the causation of present day tongue cancer appeared in Europe during the fifteenth and sixteenth centuries; namely, syphilis, tobacco, and distilled spirits (and there might also be included the habitual use of hot beverages such as coffee and tea). Although there may be considerable merit in these interpretations, nevertheless there appears to be more historic mention of cancer of the tongue than is generally believed. Furthermore, many of the ancient references to diseases of the tongue undoubtedly allude to cancer although this disease is not specifically named.

There can be little doubt that Hippocrates (B.C. 460-370), in his *Prorrheticon* refers to tongue cancer when he states that chronic ulcers of the tongue are common at the edge and urges that an examination be made for the presence of sharp teeth in contact with such ulcers. This injunction was copied almost verbatim by the encyclopedist, Celsus (fl. A.D. 178), when he observed that ulcers which arise at the side of the tongue last the longest, "and it must be looked to whether some tooth opposite the ulcer is too pointed, in which case the tooth must be smoothed down." During the next sixteen centuries, comments regarding the tendency to long duration of ulcers occurring on the edge of the tongue and their probable origin from contact with sharp teeth appear so often as to suggest plagiarism from these original statements as well as personal observations (Lanfranc, Paré, Riverius, Bell, Gibson, Walshe, Pemberton, Home, Wilson).

Galen makes no specific reference to cancer of the tongue, but he mentions "tumores duri" (hard tumors) among the organic diseases of the tongue which he

will discuss in a later book, apparently not now extant.

While it is certainly true that many of the medical writers of the first thousand years A.D. make no reference to tongue cancer, nevertheless on carefully perusing the whole texts of these medical writings, one is impressed with the fact that the lack of more specific mention of this form of the disease is in keeping with the rather vague and abstract descriptions of cancer elsewhere in the body and, as a matter of fact, of all other diseases. Aretaeus (fl. A.D. 100) does not mention cancer at all. Oribasius (A.D. 326-405) refers only to cancer of the pudenda, testes, and breasts. Rufus, in commenting on the writings of Oribasius, refers to the various forms of cancer which occur throughout the body, but omits the tongue. Paulus Aegineta (A.D. 625-680) merely states that cancer occurs in every part of the body, but most frequently in the breasts of women. It is fair to assume, therefore, that none of the latter four writers had observed a case of cancer of the tongue.

The field is not entirely barren, however, for Avicenna (A.D. 980-1037) in his *Canon of Medicine* mentions "apostema dura" (hard sore) of the tongue, which undoubtedly alludes to cancer. Abulcasis (A.D. 1013-1107) and Guy de Chauliac (d. A.D. 1368) mention cancer of the tongue briefly in passing. Ambrose Paré (A.D. 1517-1590), in a passage reminiscent of Hippocrates and Celsus, is quoted as stating that "ulcers of the tongue may be cured by the same remedies as the rest of the mouth, yet ulcers which breed on the side of the tongue endure very long," and "you must look whether or not there be some sharp tooth over against it which will not suffer the ulcer to heal, and if there be, then you must take it away with a file."

Riverius (A.D. 1589-1655) in his *Practice of Physicke* may be describing a cancer when he speaks of a case of ulcer of the tongue "which proceeded from the grating of the teeth whereupon it rested." His mention of "cancerous swelling" of the

tongue which is "known by its hardness, blueness, and pricking pain" may be taken as an example of the confusion in the diagnosis of this disease which becomes so apparent in the following two centuries.

Theophile Bonet (fl. A.D. 1684) apparently recognized that cancer occurred in the tongue, for in describing the treatment of ranula, he recommended that certain precautions be taken so as not to "endanger a cancer."

Other writers of this period who make no mention of cancer of the tongue apparently had very little experience with this disease in any part of the body. John of Vigo does not mention cancer at all. De Mondeville, although he writes at great length of the varieties and causes, the symptoms and treatment of growths in such general regions as the upper and lower extremities and upper air passages, discusses no specific anatomic form of cancer except that of the breast. In his *Select Medicinal Counsels* (1678) Fernelius' only mention of the subject is of two tumors in the left armpit which "have the show of certain cancerous wens." In his autobiography, Master Johann Dietz (1665-1738), a licensed barber and surgeon, makes no mention of cancer in any form, although he writes extensively of his professional activities. It is worthy of note that in many of the later writings where cancer of the tongue is specified, the references appear to be so casual as to give the impression that the writers considered the occurrence of this disease in the tongue in no way remarkable.

#### INTERPRETATION OF HISTORIC DATA

Although the foregoing list does not pretend to be complete, it is certainly significant that about half of these ancient writers make observations which can logically be interpreted as referring to cancer of the tongue, despite the fact that at least a third of them do not mention cancer at all. From present day knowledge, one may speculate with a considerable degree of accuracy as to which of the many

tongue lesions described were probably cancer.

Only the most incredulous skeptic will doubt that the terms "tumores duri" and "apostema dura," as employed by Galen and Avicenna, refer only to cancer. There are other somewhat ambiguous references which include chronic ulcers, ulcers which arise on the edge of the tongue, and corrosive ulcers. If we assume that the diseases to which man is now subject have not markedly changed in their nature, symptoms, and clinical course since that period, the most common chronic ulcers of the tongue would have been (as they are now), in the order of their frequency, cancer, tuberculosis, and syphilis. The other more acute and painful ulcers of the tongue of shorter duration (traumatic, herpetic, and simple inflammatory), being self-limited, would have caused little concern either to the physician or to the patient. It would surely be illogical to assume that tuberculosis and syphilis, rather than cancer, were the most common causes of these hard chronic ulcers and tumors of the tongue so often mentioned in the early literature. Moreover, the repeated reference to the teeth as an inciting cause of these lesions is further evidence of their probable malignant character, for cancer of the tongue, arising at its most common site in the middle third of the lateral border, would have suggested then, as it does now to both the patient and the physician, an origin from dental trauma.

The shorter life expectancy in the early Christian and medieval eras as compared to the modern would also undoubtedly influence the incidence of cancer, which is mainly a disease of late middle and old age. The average length of life in the first few centuries A.D. ranged from twenty to thirty years, and by the eighteenth century in Europe had increased only to forty years. Today the life expectancy of white males in the United States at birth is fifty-nine years. In a recent study of about 550 consecutive cases of tongue cancer at the Memorial Hospital in New York, it was

found that the average age of the patients was 58 and that only 3 per cent of the cases occurred in patients below the age of 39. Under these conditions, a relatively small percentage of people could have lived into the cancer age during the early Christian and medieval eras and, therefore, as compared to the present, the actual number of lingual cancers may have been small. It is entirely possible, however, that in these early periods cancer of the tongue occurred among people 58 years of age about as frequently as it does today.

At the present time, cancer of the tongue and of the lip have about an equal incidence. It should therefore be significant that except for two or three isolated references to cancer of the lip and of the tonsil, lingual cancer is the only intraoral form of this disease specifically mentioned in these early writings. In the final analysis, the infrequent historic mention of tongue cancer should probably not be interpreted as indicating so rare an incidence as has been suggested by many writers.

#### INFLUENCE OF RELIGIOUS SUPERSTITIONS

From earliest times, the tongue has been associated in the public mind with the production of speech. Until the modern era, therefore, any affliction of this organ, with the attendant speech disability, was likely to be ascribed to divine punishment for such heinous crimes as heresy, blasphemy, or clerical *lèse majesté*.<sup>\*</sup> These

<sup>\*</sup> As the result of such beliefs, excision of the tongue was the penalty often considered suitable for those who dissented from the established religious opinion. This mutilation was intended to prevent any further utterance of heresy. The executioner drew the tongue from the mouth, usually by a sharp hook, and cut off the protruding portion from below upward. Sometimes the first step in excision was to nail the tip of the tongue to a tree.

The most famous case is that of the sixty Christian confessors of Tipasa whose tongues were excised by order of the Vandal king, Hunneric, in 484 A.D. Immediately after the operation it was noted that many of these martyrs were able to speak, and a controversy arose which raged for centuries concerning the supposedly miraculous return of the power of speech. Victor, an African bishop, wrote a report of the event within two years after its occurrence. Procopius of Caesarea saw some of the victims years later and, in

practices and superstitions would naturally contribute to the failure to record many of the tongue disabilities which did occur as the result of natural disease phenomena.

In 1672, Paul de Sorbate of Germany published a case report, that of Baron Vertemali, who, it is related, recognized with great penitence shortly before his death "that the cause of his cancer (of the tongue) was divine punishment because he so often abused the clergy." Bonet (1620-1689) also comments on the supernatural significance of this case. Such a superstition is also apparent in the case of Nestorius (fl. A.D. 430), a Syrian bishop who promulgated the doctrine of monophysism (the single as opposed to the dual nature of Christ). His enemies triumphantly related that his tongue was eaten by worms as a divine punishment for his heresy. History does not record how the learned doctors of divinity finally came to agreement concerning the number of Christ's natures, but it is not unreasonable to suppose that among Nestorius' attending physicians there may have been at least one skeptic who, too prudent perhaps to risk excommunication by voicing his opinions, nevertheless suspected (as, no doubt,

support of the miracle theory, reported that the tongues were cut out "as low down as the throat," but that with the exception of two who had "allowed themselves to hold converse with abandoned women" and therefore "ceased to speak," none showed any effects of his punishment. Twistleton, in an admitted attempt to discount the "miraculous element in the history of the African confessors," gathered together a series of cases of individuals who had lost their tongues by disease or excision, or who had been born without them, and who were still able to speak. Among these were a group of French Protestants who were condemned to have their tongues out before being led to the stake. Immediately after the operation one of them repeated three times, "Le nom de Dieu soit beni." It is a well known fact today that after excision of the tongue as far back as the anterior tonsillar pillars, the remaining stump and the musculature of the floor of the mouth develop an unusual range of motion, so that the functions of the tongue in articulation and in swallowing are retained to a surprising degree. Brodie, furthermore, pointed out that the early executioners, in general, removed a much smaller portion of the tongue than they thought. In any event, it is highly probable that the recoveries from these early excisions of the tongue paved the way for early attempts at glossectomy in the treatment of diseases of the tongue.

does the reader) that the unfortunate churchman died of tongue cancer.

#### CONFUSION IN DIAGNOSIS\*

During the eighteenth century, one finds numerous references and reports of operations on lingual tumors, many of which were obviously not cancer. It was not until the time of Virchow (1821-1902) that definite attempts were made to distinguish clinically between gumma and cancer of the tongue. At about the same time, Anger (1872) called attention to the frequency with which these two lesions were confused. He stated that the natural progression of lingual cancer under anti-luetic treatment was often erroneously ascribed to mercurial glossitis, so that all treatment was stopped to await the subsidence of this supposed complication while the cancer was left, undiagnosed and undisturbed, to pursue its natural malignant course.

A lesion occasionally confused with carcinoma was lymphangioma, which was probably the case in the celebrated operation done by Louis in 1759 "*d'un seul coup de ciseaux*," and sometimes referred to as the first case of tongue cancer operated upon. Lymphangioma also appears to be the most likely diagnosis in some of the cases reported by Home and Inglis. An error in diagnosis, even more obvious, is the second case mentioned by Louis and cited by many others, that of a girl of 20 years of age who "had lost her tongue at the age of 4 by cancer." The literature contains several references to children

whose tongues became gangrenous and sloughed away as the result of smallpox, and it is possible that this girl was the victim of such a disease.

Up until the latter part of the nineteenth century, most cervical lymphadenopathies were apparently grouped under the general term "*scrofula*," especially if they were associated with "*eruptions*" of the skin or oral mucous membranes. Under such conditions it is obvious that errors in diagnosis would be likely to occur in the cases of oral cancer in which cervical lymphadenopathy appeared as the first or as one of the early symptoms. In these cases, the small primary lesion of cancer, either in the skin or in the mucous membrane, was probably often classified as an "*eruption*" and the metastatic cervical node diagnosed as "*scrofulous*."

#### INTRODUCTION OF NEW ETIOLOGIC FACTORS

If one depended entirely upon the number of cases reported in the literature for proof of the incidence of tongue cancer, one would be forced to conclude that there was a definite increase in the occurrence of this disease about the seventeenth century. The possible relationship between an apparent increase in lingual cancer and the introduction of new and competent etiologic factors at this time has been made the subject of considerable speculation. Curiously enough, there is indisputable evidence that several such factors were introduced or became prevalent during this period; namely, syphilis, tobacco, and certain dietary changes.

At the present time, more than one-third of all patients with tongue cancer also have syphilis, a fact which indicates a highly significant causal relationship. Whether or not one subscribes to the theory of pre-Columbian syphilis in Europe, it is a well attested historic fact that this disease became epidemic on the Continent during the fifteenth and sixteenth centuries to such an extent that a large percentage of the general population was afflicted. It follows, therefore, that

\* Much of this confusion in diagnosis was due to a lack of uniform terminology, so that many diseases were considered to be similar to but not identical with cancer. Walshe, in 1857, in an attempt at systematization, divided all cancer into three classes; namely, colloid or jelly-like cancer, scirrhus or hard cancer, and encephaloid or soft cancer. Under these "*species*" he listed thirteen "*varieties*." In connection with his classification of cancer, Walshe mentioned thirty-three "*synonyms*" (as, for example, *struma fungosa*, *fungus haematodes*, *cerebroform degeneration*, *milk-like tumor*, *galactomyces*, *scirrhoma*, etc.) of the "*species*" of cancer, which he condemns as being a "*diversity of names*" which "*by no means implies a corresponding diversity of things*."



there must have been a marked increase in syphilitic glossitis, a form of chronic irritation which today is the most important single etiologic factor in the production of lingual cancer.

Another form of chronic irritation universally considered important in the present day etiology of tongue cancer is tobacco, the use of which was introduced into England from America in 1586. The habit became widespread on the Continent in the following century. References to the association of pipe smoking with cancer of the tongue and of the lip have been so long and so frequently made as to become classical and, as with certain other conventional beliefs, their importance has probably been exaggerated. In any event, the influence of tobacco in lingual cancer today is probably often overemphasized, especially with regard to cigarettes or the moderate indulgence in other forms. The percentage of patients with tongue cancer who use tobacco is of little significance from an etiologic standpoint unless this figure is compared with the percentage of addiction in the normal healthy adults.

The habitual consumption of beverages of high alcoholic content is sometimes considered competent to produce lingual or other forms of intraoral cancer. It is believed that about 800-900 A.D. the Arabs brought to perfection the art of distillation, although they themselves may not have invented it. The word "alcohol" was coined by them. It is not definitely known when the use of this more potent liquor became common, but during the reign of Elizabeth (1558-1603), a tax was first placed upon distilled alcoholic beverages. One might be justified in supposing that the first levy of such a tax followed a marked increase in the use of these distillates, for it is obvious that an alert financial adviser of the good queen would have been quick to take advantage of any new and profitable source of revenue. The alcoholic content of the fermented beverages used before the introduction of

distillation could probably have no marked irritating effect upon the tongue, but there is no doubt that the habitual use of liquors containing 40 to 50 per cent alcohol (whiskey and brandy) can produce such an effect on the oral mucous membranes.

In the sixteenth and seventeenth centuries, coffee and tea were introduced into Europe, and though at first they were very expensive, their use soon became widespread. These were probably the first very hot beverages to be habitually consumed by man, and it is reasonable to believe that such a thermal irritant to the oral cavity repeated several times daily over a period of years might exert a definite carcinogenic action. Another dietary factor which probably became significant during the Middle Ages was the excessive use of highly flavored sauces and condiments made from spices, which were held in great favor to disguise the otherwise unpalatable and monotonous flavor of the poorly cooked and often poorly preserved meat which comprised the main article of diet. It was because the trade in spices was so profitable that Columbus set out to find a short route to India. The excessive use of such undoubtedly irritating condiments, as well as very hot food and drink, is frequently noted in patients with marked leucoplakia and sometimes with cancer. In all of these cases, however, it is not entirely clear that the inordinate desire for highly seasoned or hot foods has actually preceded and probably caused the development of leucoplakia. Lacking specific observations as to the previous condition of the tongue, it is almost equally possible that these abnormal cravings result from an instinctive effort to titillate the diminished gustatory sensations of the relatively insensitive leucoplakic tongue surface.

It is an undoubted fact that a more frequent reference to tongue cancer in the medical literature began late in the renaissance, coincident with the introduction of these several etiologic factors. From the available evidence, however, it is

difficult to assay their significance as compared with the more frequent recording of tongue cancer which would naturally grow out of the awakening of interest in science accompanying the renaissance, and the steadily increasing life expectancy. Astute medical observers are well aware of the fact that the apparent incidence of a given disease from time to time often varies directly with the interest manifested in it by the medical profession. Therefore, that the early physicians did not often mention tongue cancer does not necessarily indicate that the disease was unusually rare as compared to the present time.\*

#### DEVELOPMENT OF TREATMENT METHODS

Beginning with Hippocrates and continuing until the sixteenth century, cancer of the tongue was considered a *noli me tangere*. Abulcasis (A.D. 1013-1107), who noted the occurrence of several varieties of "tumors" in the mouth and throat, describes the use of the cautery for treating external cancer, and warns that in the treatment of ranula, one must be certain that the tumor is neither "livid and black" nor "hard and painless," for "if it is, do not touch it, it is cancer." Guy de Chauliac (d. A.D. 1368) speaks of corrosive ulcers in the tongue and states that "if the growth in the tongue is hard and cancerous, don't touch it to cure it." Lanfranc (fl. A.D. 1490) was probably speaking from an unpleasant personal experience with a case of lingual cancer when he advised that "if an ulcer (of the tongue) be melancholic, which you know by the livid or black color, don't touch it."

\* A questionnaire was recently sent by the author to ten general practitioners without hospital connections who have practiced in rural communities for periods of twenty-five to forty years. About half of these physicians stated that they had never observed a single case of cancer of the tongue in their own practices, and only one had observed more than two cases. Certainly the rural general practitioners of today are far superior to ancient and medieval physicians by virtue of training and cumulative experience, and since they rarely encounter lingual cancer, it seems irrelevant to the study of the comparative incidence that so many of the earlier medical writers fail to mention it.

*Early Attempts at Glossectomy.* By the beginning of the eighteenth century, there had already been several attempts at surgical removal of lingual tumors. Marchetti in 1664, using the cautery, was probably the first to attempt the extirpation of cancer of the tongue. In 1676, Wiseman reported operating upon two patients with cancer of the tongue, using the cautery, both of whom later died with metastases. Following these two glossectomies, the use of the cautery in the treatment of lingual cancer seems to have fallen into disrepute, and it was not until the beginning of the twentieth century that it came again into general use. Today it is considered one of the most practical methods.

Gemy in 1787 reported the postoperative recovery of a patient following the removal of a carcinomatous tumor from the side of the tongue, but Richard in 1852 made the statement that there was at that time no authentic case of cure of cancer of the tongue in all the literature. Pemberton in 1867 concurred in Richard's statement with the comment, "there are no remedies with which we are at present acquainted that exercise any influence in retarding the progress of this disease. . . . Our only means of arresting the progress of cancer of the tongue consists in resorting to an operation. Under the best aspects the treatment of cancer of the tongue by operation can be looked on only as a palliative measure, the tendency after all operative interference, however well considered, being to a speedy relapse."

The difficulties attendant upon the early attempts at surgical removal of the tongue can well be appreciated, and the operation seems always to have challenged the efforts of the more courageous surgeons. Louis, in his plea for earlier and more frequent performance of glossectomy when indicated, chides Morgagni for advising against the operation, and states that "il n'est pas exercé par des hommes timides." Harris, in 1720, recognized the danger accompanying excision of the

tongue, but nevertheless seemed to feel that perhaps the operation might at least have some psychotherapeutic merit for

to describe the removal of an undoubted epithelioma preceded by the ligation of the lingual artery. Robert, in 1856, re-

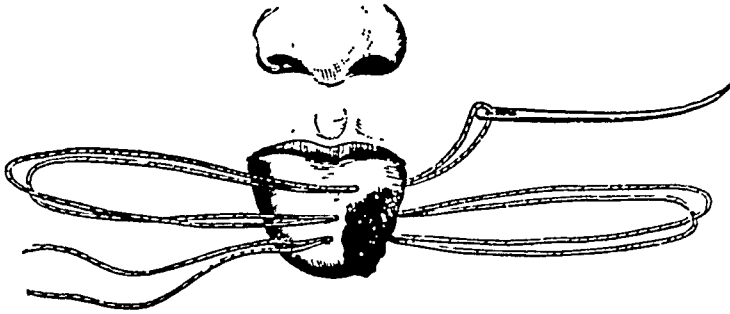


FIG. 1. Application of ligature for removal of cancer of the tongue (Erichsen). By cutting off the needle and cutting through the loops, the ligatures could be tied separately so as to encompass the entire diseased portion which, according to reports, sloughed off eight to ten days later.

he observed philosophically that "if anyone is exceedingly wearied with such tumors (of the tongue), and especially dejected in mind, whilst he is prepared to bear equably whatever may happen, he should not be denied the trial of the operation of excision." Clarke (1873), in the same vein, said of the operation that "though it may only be temporary, relief is given both to the body and mind of the sufferer."

Although hemorrhage is not often specifically mentioned in the earlier reports of surgical excision of the tongue, it is probable that this complication was the main cause of the timidity of which Louis accused Morgagni. When hemorrhage was controlled by packing and the application of caustics or "tincture of iron" ( $\text{FeCl}_2$ ), local oral sepsis figured as a prominent complication and was frequently followed by pneumonia. Butlin in his first edition discusses at some length the dangers of these early operations with their troublesome and frequently fatal pulmonary complications. He believed that "the pneumonia is due, in a large majority of instances, to the inhalation of foul gases from the decomposing wound." The Miraults, in 1813, introduced the ligation of the lingual artery before they removed a "fungating ulcer" from the tongue of a man, but Roux, in 1839, was the first

recorded two cases in which severe hemorrhage following excision of the tongue was controlled by applying the handle of a spoon to compress the tongue, in the same manner as when examining a sore throat.

Beginning with Louis, the surgical aspect of glossectomy for a variety of conditions, including cancer, was emphasized rather than the clinical features of the disease, so that little progress in the study of lingual cancer was made until the time of Anger in 1872 and Butlin in 1885, both of whom published monumental works on this disease. Butlin's historic interest in lingual cancer seems in the main to have followed the surgical development of glossectomy. In his later editions, the historic details of the evolution of this procedure are rather extensively recorded.

*Glossectomy by Ligature.* At about the beginning of the nineteenth century, operations upon the tongue became more extensive than they had been previously, and postoperative hemorrhage, both immediate and late, called for some other method of excision than by scalpel. The slow strangulation and necrosis of the part by several ligatures encompassing the tumor area was one means introduced to prevent immediate hemorrhage. Home is believed to be the first to use this method, and in 1805 he reported six cases of his own or of others, five of which were probably cancer.

The technique of this procedure as described by Home was to draw the tip of the tongue from the mouth and pierce under the mandible through incisions or stab wounds in the submaxillary or suprahyoid regions in such a way as to



FIG. 2. The chain ecraseur (Holmes). This instrument, an elaboration of the principle of the ligature, used either a cord, a wire, or a chain which could be drawn tight by means of a screw, and provided for the more rapid strangulation and cutting through of the diseased portion of the tongue. (See Figs. 4 and 5.)

it from its superior to the inferior surface with a needle threaded with a double ligature. (Fig. 1.) The needle was then cut off, one ligature tied in the sagittal and one in the coronal plane over the surface of the tongue so as to strangulate a wedge-shaped area containing the tumor. The operation was, of course, performed without anesthesia, but after the ligatures were tied the patient was usually given tincture of opium. If the ligatures were tight enough, the strangulated portion soon became necrotic and slough separated

encircle the base of the tongue. Mirault in 1833 placed a mass ligature deeply in the floor of the mouth in an attempt to ligate the lingual arteries prior to glossectomy. Despite some immediate technical difficulties and the subsequent failure of one of the ligatures to hold, Mirault reported that "*la tumeur s'atrophie et disparut entièrement.*"

*The Ecraseur.* The plain ligature method was sometimes uncertain in its application, and in any event required several days for the separation of the

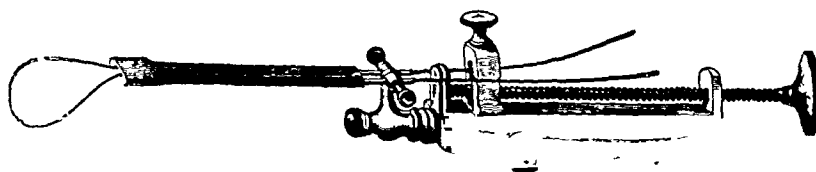


FIG. 3. The galvanic ecraseur (Erichsen). In this instrument the wire loop was heated by an electric battery, thereby combining the cautery with a crushing action. Judging from the rather infrequent mention of the instrument, it is probable that its use was more theoretical than practical.

within seven to nine days. Hilton and, later, Moore recommended division of the lingual nerve as the first step in the operation, as well as for the palliative relief of pain.

Inglis in 1805 reported the removal of two supposed cancers of the tongue by ligature. From the clinical descriptions, the long duration, and the presence of one in a girl of 10 years of age, one is led to the conclusion that both were probably lymphangioma. Cloquet, in 1827, applied the ligature from below, introducing it

strangulated portion, so that about the middle of the nineteenth century the ecraseur (crusher), an elaboration of the same principle, was introduced by Bell. By this method the operation could be completed in a much shorter time. This instrument, in the words of Clarke, consisted "of a chain or wire disposed in the form of a running loop at the end of a shaft. This shaft is provided with a suitable handle and with a powerful screw, by means of which the loop can be drawn tight." (Fig. 2.) The part of the tongue to

be removed was encircled by the loop, and by gradually increasing the tension a part of the organ was strangulated and cut

wire I use is a strand of wire rope used for park fencing." (Fig. 4.)

Baker modified the ecraseur method by

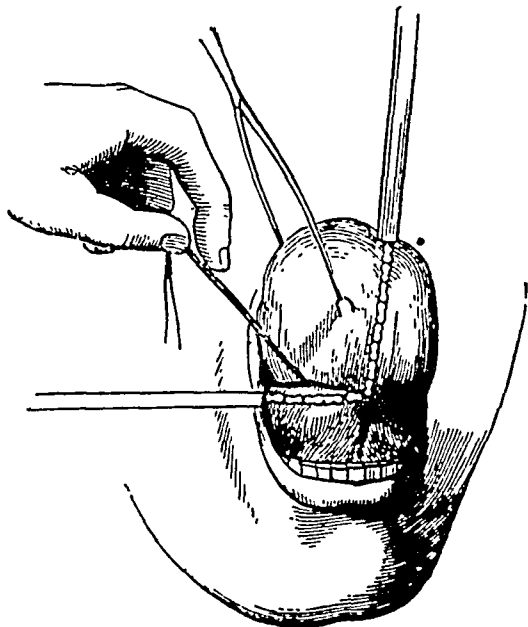


FIG. 4. Removal of the anterior portion of the tongue by the application of two ecraseurs (Erichsen). The ligature in this case was used both for traction and to prevent the ecraseurs from slipping forward.

through, thereby supposedly preventing any serious hemorrhage. Chaussaignac described an elaborate technique by which the chain was introduced through stab wounds at the upper point between the submental and suprahyoid regions so as to encircle the whole tongue proximal to the tumor.

Boyer stated that with this device it was possible to remove the anterior portion of the tongue, the whole, the lateral half, or any tumor which developed on the superior or inferior surfaces in the angle formed by the base of the tongue and the floor of the mouth, although he did not cite any cases of his own. Middeldorff, by the use of a galvanic battery (Fig. 3), heated the loop of such a chain, thereby combining the advantages of the cautery with the crushing action of the ecraseur. Barwell developed an operation for excision of the tongue using two ecraseurs with soft iron wires. He specified that "the

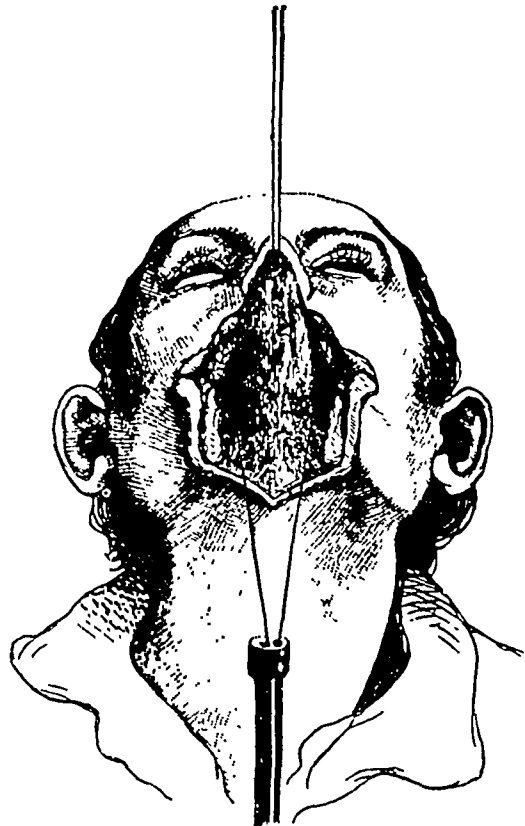


FIG. 5. Sedillot's approach for operations on the tongue by splitting the lower lip and jaw in the midline (Erichsen). The tongue was drawn forward and the anterior portion removed by a wire ecraseur.

using whipcord rather than chain or wire for the noose, after preliminary freeing of the tongue from its attachment to the genial tubercles and from the anterior tonsillar pillars. In order to obtain more space, he sometimes divided the cheek as in Jaeger's operation. The noose was placed behind needles thrust into the tongue well back of the diseased portion, in order to prevent its slipping forward over the growth. One cannot but be impressed by the fortitude of those patients who submitted to ordeals so protracted and painful before the beneficent discovery of general anesthesia.

*Escharotics.* Although escharotics had long been used for external cancer, it remained for Girouard in 1857 to apply

such substances to tongue cancer. He introduced pieces of zinc chloride into stab wounds surrounding the tumor and claimed good results in several cases. Maisonneuve in 1858 also recommended this procedure. Arnott in 1858 reported a case of tongue cancer treated by injections of acetic acid in water, supplemented with surface applications of undiluted acid. At the end of a month "scarcely any hard base existed, but it has extended toward the tip of the tongue." In 1861 Bright recorded a case of lingual cancer treated successfully by repeated applications of copper nitrate. Clarke, however, in 1873 reported that caustics were no longer in general use for treating cancer of the tongue.

*Introduction of Systematic Excision.* Beginning with Langenbeck who, in 1819, introduced the V-shaped excision and closure, surgical excision by the scalpel developed coincident with the continued use of the ligature, ecraseur, and escharotics. In 1831, Jaeger divided the cheek to obtain better access to the tongue before excising it, and Roux (d. 1836) and Sedillot (1844) divided the lower lip and the lower jaw itself, for the same purpose. (Fig. 5.) Regnoli (1839) opened the floor of the mouth from below by a curved incision from the middle of the hyoid bone to the chin, and the tongue was then drawn through this opening for its excision. (Fig. 6.) Billroth, Kocher and von Langenbeck, during the latter part of the nineteenth century, also developed approaches through the submaxillary and suprahyoid regions, and these early pharyngotomies still survive in the present day laryngopharyngotomy of Trotter and of Hofer and Hajek. Unless the latter ambitiously conceived procedures be taken as heralding an even more radical era for the surgical treatment of lingual cancer, the zenith of radical surgery for cancer of the tongue was reached in the late nineteenth century with the perfection of the technique of general anesthesia and of aseptic surgery.

Clarke, in 1873, advised against the use of a general anesthetic in glossectomy per-

formed with a scalpel, but Whitehead (1881), with the assistance of chloroform anesthesia, systematized the operation

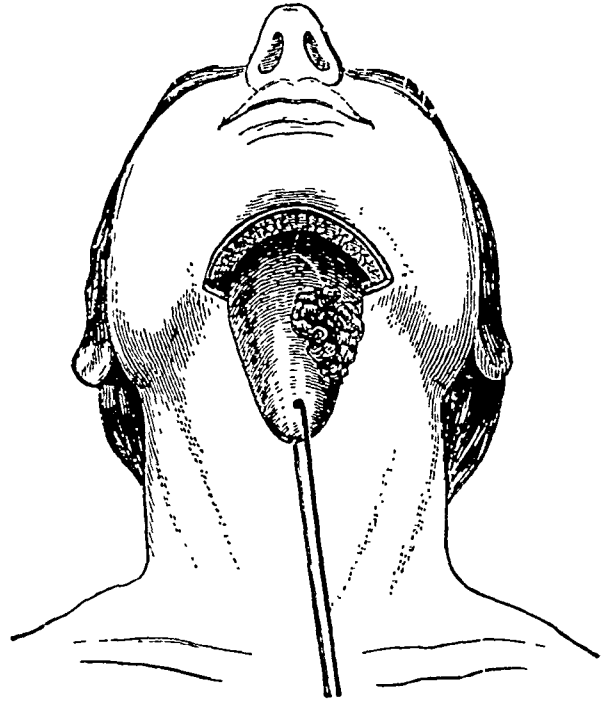


FIG. 6. Regnoli's method of exposure for glossectomy (Erichsen). A curved incision was made in the submental region along the inner border of the mandible and through the floor of the mouth. The tongue was then drawn through this opening for excision. The particular advantages of this approach are not entirely clear, and were probably mainly theoretical.

done through the open mouth without splitting either the cheek or the jaw. By careful attention to anatomic details, this operation was unusually successful for that period and employed none of the crude and deforming procedures previously recommended. Butlin, from 1881 to 1908, operated upon 197 patients with cancer of the tongue, and fifty-five of them lived from three to twenty-two years without recurrence.

*Radiation Methods.* Shortly before the turn of the nineteenth century, two new agents were discovered which later came to play a most important rôle in the treatment of cancer. Roentgen, in 1895, discovered x-rays, and two years later the Curies discovered radium. It was not long until the curative effects on cancer of both x-ray and radium had been demonstrated.

In 1902, Beck mentioned cancer of the tongue as being suitable for treatment by x-rays, and in the same year Cleaves suggested the use of an x-ray tube with a target in a tubular projection which could be inserted into cavities, as for example in the treatment of cancer of the mouth, rectum, cervix and vagina. This idea was soon abandoned because of the difficulty of insulation which resulted in burns of several patients, but Cleaves' original suggestion has been developed more recently by Chaoul.

A more detailed report of x-ray therapy in cancer of the tongue was published in 1902 by Dickson, who had treated one case by daily divided doses over a period of three weeks, through the open mouth, shielding cheek and lips. Pratt, in discussing Dickson's paper, reported a case of lingual cancer treated with x-ray, using a celluloid speculum to hold the lips apart.

In 1903, Engman reported a case of lingual cancer also treated by daily divided doses of x-ray, the first series over a period of thirteen days, the second over a period of eight days, with a week's interval between. The treatment produced a mucositis, and within a month the tongue was practically healed. A year later the patient was well. Krauss, also in 1903, treated cancer of the tongue with x-ray. In 1904, Bulkley treated two cases with radium, and Courtin and Bergonne treated one case. Hallopeau, in the same year, reported similar treatment of two cases.

In February, 1902, x-radiation for the treatment of cancer was first used in the Memorial Hospital, New York City (then called the General Memorial Hospital). In the report of that hospital for the following year, Dr. William B. Coley stated that eighty-four cases of various forms of tumor had been treated, and adds that "in the tongue cases, there have been no good results," although he does not mention the number of cases treated. Not until 1911 do the yearly reports of this hospital again mention the use of radiation in the treatment of cancer.

Dominici, in 1908, reported a case of tongue cancer successfully treated by the application of radium contained in lead tubes. He stated that the treatment was successful in only one case in which the cancer had not gone beyond the mucous membrane of the tongue to penetrate the muscular tissue. In 1909, Forssell of Stockholm began the treatment of tongue cancer by radium.

Stevenson, in 1914, appears to have been the first to employ needles containing radon or radium for interstitial use, and in 1915 he reported success with twenty-two cases of cancer, including three in the tongue. Shortly thereafter, this method was put into use at the Curie Institute by Regaud and at the Radiumhemmet by Forssell and Berven. In both of these institutions, radium element needles are still considered the most suitable interstitial applicators for the treatment of lingual cancer.

In 1917, Janeway reported the treatment by radium of forty-eight patients with cancer of the tongue at the Memorial Hospital, the first one on August 28, 1914. Radon capsules attached to the tongue by means of barbed hooks were used in treating the first cases. These devices were soon found to be unsatisfactory, and were replaced by platinum tubes of radon tied or sewed to cotton cloth and held in place upon the tumor by gauze packing. Janeway found it difficult to maintain any of these devices in accurate approximation to the tumor. In some instances, he insisted that the patient hold out his tongue during the entire treatment, which often extended over several hours. A nurse was on duty beside the patient throughout the application to give moral support during the ordeal, and to make certain the applicator remained in proper position.

In the 1917 Radium Report, Janeway refers to Duane's suggestion for the construction of very fine short glass tubules for interstitial insertion, but the so-called "bare tubes," or glass seeds, did not come into use until 1918. From that time on,

they were employed by Janeway and Quick in the treatment of tongue cancer. A review of Janeway's case reports indicates that with his method of radium treatment of early tongue cancer by contact application, surface healing of the tumor was often followed by recurrence. He seemed to be particularly impressed by the fact that such recurrences were likely to take place on the borders of the lesion, and discussed the advisability of treating an area larger than the apparent size of the tumor itself. His difficulties are illustrated by his statement (in 1917) that "by the time cancer of the tongue becomes over one centimeter in diameter, the possibility of healing it with radium becomes uncertain."

About 1920, the endotherm knife was developed on the basis of DeForrest's earlier discoveries that a rapidly oscillating electric current would cut. This device has been favored at times by Wyeth and others almost to the exclusion of other agents in the treatment of intraoral and accessible cancer.

At the time of this writing, radon gold seeds or radium needles of small caliber and content are the most widely used form of applicators for interstitial radiation, and are often combined with surgical removal by cautery or endothermy for the treatment of the primary lesion of tongue cancer. The most recent development in the treatment of intraoral cancer is the reintroduction of peroral x-radiation employed in conjunction with one or more of the above-mentioned methods.

#### SUMMARY AND CONCLUSIONS

Cancer of the tongue is almost the only form of intraoral cancer which is even vaguely mentioned in the early medical writings, and most of these early references are by inference only. So far as is known, the first definite case report of lingual cancer appeared in the medical literature in 1635. Subsequent case reports and clinical descriptions of this disease were made with increasing frequency during the next two centuries, coincident with the introduction

of certain new etiologic factors competent to produce irritation in the tongue. The question might be raised, therefore, whether the introduction of these several new etiologic factors was the direct cause of an actual increase in lingual cancer or whether they were simply coincident with a more frequent reporting of the disease during the scientific awakening of the renaissance.

Surgical excision of the tongue was introduced in the seventeenth century, but undoubtedly many lesions operated upon were not cancer. These first attempts at glossectomy for a variety of diseases were probably suggested by the recovery, often considered miraculous, following excision of the tongue as punishment. The early operations for cancer were accompanied by several serious complications, and during the nineteenth century several new methods and modifications were devised to obviate these complications, including the use of the ligature, the cautery, the ecraseur, escharotics, ligation of the arterial blood supply and, finally, toward the close of the nineteenth century, the application of radium and x-ray.

#### REFERENCES

- ABULCASIS. Translation of LeClerc. Paris, 1861, ch. 35, b. 2 (Liev. 2).
- ANGER, THEOPHILE. Du cancer de la langue. Paris, 1872.
- ARNOTT, JAMES. On the Painless Extirpation of Cancerous Growths by Congelation and Caustic. London, 1858. John Churchill.
- ASHHURST, J. Principles and Practices of Surgery, 6th edition. Philadelphia, 1893. Lea.
- AVICENNA. Canon of Medicine. Liber iii, fen vi, cap. 14.
- BARWELL, R. Brit. M. J., 1: 697, 1889.
- BECK, C. New York M. J., 75: 881, 1902.
- BELL, B. A System of Surgery. Edinburgh, 1786. iv, sec. iii, p. 329.
- BERVEN, E. Acta radiol., 10: 3, 1929.
- BILLROTH. Arch. f. klin. Chir., p. 681, 1862.
- BLEYER, J. M. New York State J. Med., 53: 245, 1896.
- BONET, T. A Guide to the Practical Physician. London, 1684.
- BONET, T. Medicine Septentrionalis Collatitia. Geneva, 1: 302, 1685.
- BOYER, J. E. Du cancer de la langue. Paris, 1865.
- BRETT, W. R. A Short History of Some Common Diseases. London, 1914. Oxford University Press.
- BRICKNER, W. M. Internat. J. Surg., 16: 303, 1903.
- BRIGHT, J. W. Cancer, Its Classification and Remedies. Philadelphia, 1871. S. W. Butler.



- BUCKLEY, D. L. *J. A. M. A.*, 40: 180, 1904.
- BUTLIN, H. T. *Diseases of the Tongue*, 1st edition. London, 1885. Cassell and Co.
- BUTLIN, H. T. *Brit. M. J.*, 1: 1, 1907; 1: 462, 1909.
- BUTLIN, H. T., and SPENCER, W. G. *Diseases of the Tongue*, 2nd edition. London, 1900. Cassell and Co.
- CELSUS. *De Medicina*. Trans. by J. W. Underwood, London, 1830.
- CHAOUL, H. *Strahlentherapie*, 50: 446, 1934.
- DE CHAULIAC, G. *Chirurgia Magna*, 1363.
- CHAUSSAIGNAC. *Traité de l'écrasement linéaire*. Paris, 1856.
- CLARKE, W. F. *Diseases of the Tongue*. London, 1873. Renshaw.
- CLEAVES, M. J. *Advanc. Therap.*, 20: 564, 1902.
- COURTIN ET BERGONIE. *Gaz. hebdomadaire de médecine et de chirurgie*, 25: 18, 1904.
- DÉLÉPINE, S. *Brit. M. J.*, 1: 559, 1896.
- DICKSON, C. J. *Advanc. Therap.*, 21: 9, 1903.
- DOMINICI, H. *Ass. franc. p. l'étude du cancer*, p. 124, 1908.
- DUBLIN, L. I., and LOTKA, A. J. *Length of Life*. New York, 1936. Ronald Press.
- EBER'S PAPYRUS. Trans. by B. Ebell. London, 1937. Oxford Univ. Press.
- ENGMAN, M. F. *Interstate M. J.*, 10: 377, 1903.
- ERICHSEN, J. E. *The Science and Art of Surgery*, 8th ed. Philadelphia, 1884. Henry C. Lea's Son & Co.
- FERNELIUS, A. *Select Medicinal Counsels*. London, 1678. G. Sawbridge. In *The Practice of Physick*, by Riverius.
- FITZWILLIAMS, D. C. L. *Tongue and Its Diseases*. London, 1927. H. Milford.
- GALEN. *Opera*, Basel, 1549, vol. iv; de *Locis Affectis*, Liber iv, cap. ii, p. 88 c.
- GARRISON, F. H. *History of Medicine*. Philadelphia, 1924. Saunders.
- GEMY, A. J. *de med., chir.*, 71: 287, 1787.
- GIBBON, E. *Decline and Fall of the Roman Empire*, vol. II. New York, 1932. Modern Library.
- GIBSON, W. *Institutes and Practices of Surgery*, Vol. 1, p. 276. Philadelphia, 1825.
- HALLOPÉAN, M. *Bull. acad. de méd.*, 51: 555, 1904.
- HARMER, W. D. *Brit. J. Surg.*, 15: 661, 1926.
- HOLMES, T. *Surgery: Its Principles and Practice*. Philadelphia, 1889. Lea Bros.
- HOME, E. *On Cancer*. London, 1805. W. Bulmer and Co.
- INGLIS, A. *Edinburgh M. & S. J.*, 1: 34, 1805.
- JEAGER. *De extirpatione linguae*. Erlangen, 1832.
- JANEWAY, H. H. *Am. J. Roentgenol.*, 5: 414, 1918.
- KOCHER. *Deutsche Ztschr. f. Chir.*, 13: 134, 1880.
- KRAUSS, W. *Memphis M. Monthly*, 23: 416, 1903.
- LANFRANC. *La Chirurgia*. Lyon, 1490.
- LANGENBECK, C. *Biblioth. f. Chir. v. Augenheilk.*, 2: 487, 1819.
- LOUIS, M. *Memoire physiologique et pathologique sur la langue*. *Mém. acad. roy. de chir.*, 5: 486, 1774.
- MAISONNEUVE, J. *Compt. rend. Acad. sc.*, 57: 831, 1865.
- MIALL, B. *Tr. of Master Johann Dietz*. New York, 1925. E. P. Dutton.
- MIDDELDORPF, A. T. *Schmidt's Jahrb.* 107, 260.
- MIRAULT, J. *Arch. Gen.*, 6: 5, 636.
- DE MONDEVILLE, H. *Chirurgie*. Paris, 1895, p. 476.
- MORGAGNI. *De Sedibus et Causis Morborum*, Vol. IV, epistol. L. artic. 26.
- NEWMAN, J. H. *An Essay on the Miracles Recorded in the Ecclesiastical History of the Early Ages*. London, 1843. Rivington.
- ORIBASIIUS. *Synopseos, liber vii, cap. xi*, Bindoni, 1576.
- PARÉ, A. *Chirurgion Workes*. London, 1634.
- PAUL OF AEGINETA. *Epitome*. Venice, 1528.
- PEMBERTON, O. *Clinical Illustrations of Cancer*. London, 1867. Longmans, Green, Reader & Dyer.
- POWER, D'ARCY. *Selected Writings 1877-1930*. Oxford, 1931. Clarendon Press.
- QUICK, D. J. *A. M. A.*, 77: 436, 1921.
- Radium Report of the Memorial Hospital*. New York, 1917. Hoeber.
- READ, ALEXANDER. *The Chirurgicall Lectures of Tumors and Ulcers*. London, 1635. Treat. 2, lect. 26, p. 313.
- REGAUD, C. *Am. J. Roentgenol.*, 21: 1, 1929.
- RICHARD, A. *Soc. anat.*, 28: 356, 1852.
- RIVERIUS, L. *Practice of Physick*. London, 1668.
- ROBERT, H. *Le cancer de la langue*. Paris, 1856.
- ROBINSON, V. *Pathfinders in Medicine*, 2nd ed. New York, 1929. Medical Life Press.
- RUFUS. *Opera* 45, ii.
- RUSSELL, J. C. *Human Biology*, 9: 588, 1937.
- SPENCER, W. C., and CADE, S. *Diseases of the Tongue*, 3rd ed. Philadelphia, 1931. Blakiston.
- STEVENSON, C. *Brit. M. J.*, 2: 9, 1914.
- TWISLETON, E. *The Tongue Not Essential to Speech*. London, 1873. John Murray.
- WHITEHEAD. *Tr. Internat. Med. Congress*, 2: 461, 1881.
- WILSON, G. *Life of Dr. George Reid*. Sutherland and Knox, 1852. Edinburgh.
- WISEMAN, R. *Chirurgicall Treatises*. London, 1692.
- WOEFLER, A. *Arch. f. klin. Chir.*, 26: 314, 1881; 27: 419, 1882.
- WYETH, G. A. *Ann. Surg.*, 83: 583, 1926.



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